

qMRI analysis of cartilage and bone.













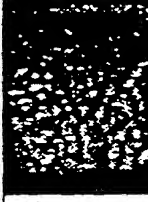

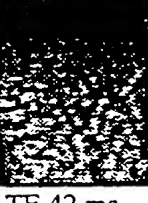







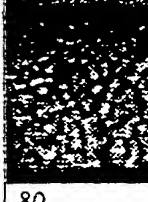

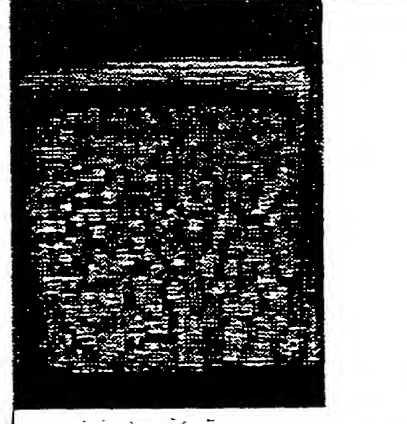
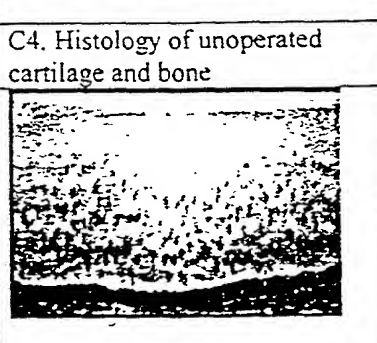
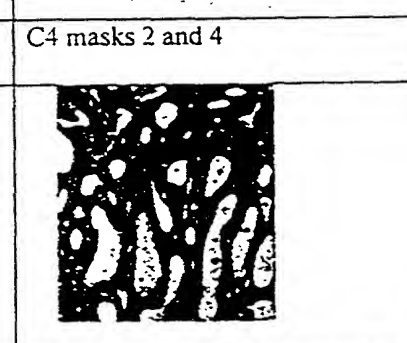
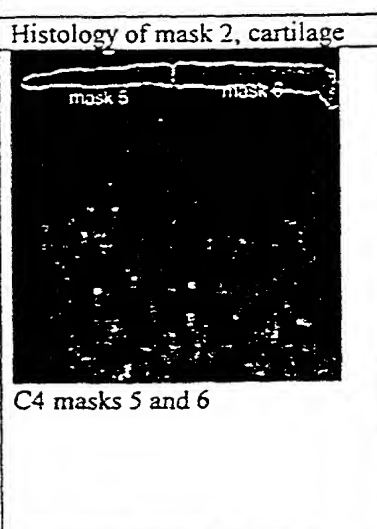
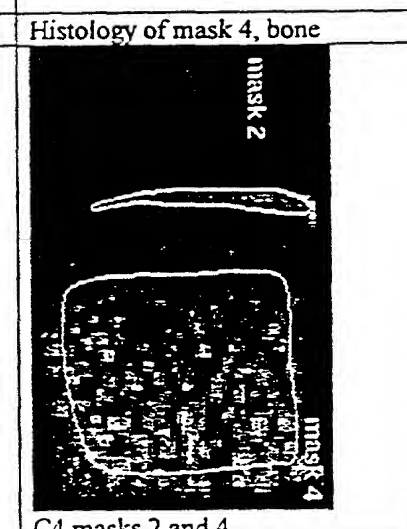
T2 Relaxation TR 5000 ms	T2 Relaxation (continued)	T1 Relaxation TE 6ms	Msat/M0 B1(0.15G)-10kHz	ADC-pulsed field gradient
 TE 6ms		 TE 5000 ms	 0 ms saturation	 0
 TE 12 ms		 TR 2500 ms	 20 ms saturation	 20
 TE 18 ms	 TE 36 ms	 TR 1500 ms	 50 ms saturation	 40
 TE 24 ms	 TE 42 ms	 TR 1000 ms	 100 ms saturation	 60
 TE 30ms	 TE 48 ms	 TR 500 ms	 200 ms saturation	 80

Figure SRL 1

A complete set of MRI scans from the qMRI analysis of one osteochondral plug (C4) showing the sequence of data acquisition and change in signal intensity of the cartilage.

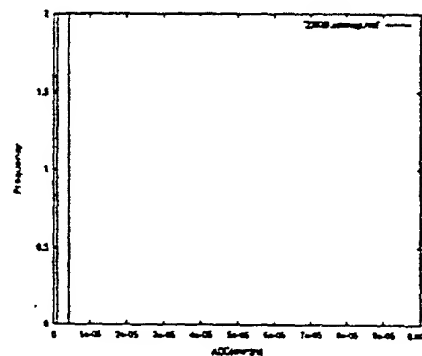
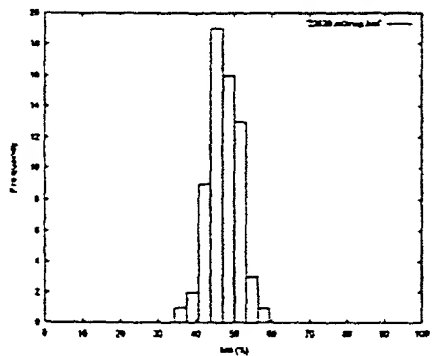
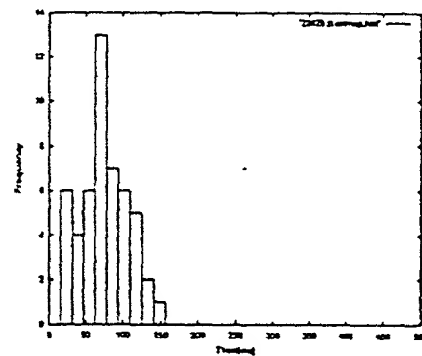
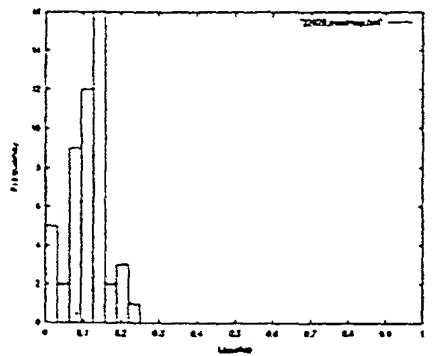
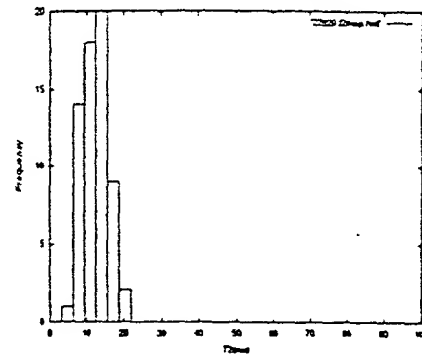
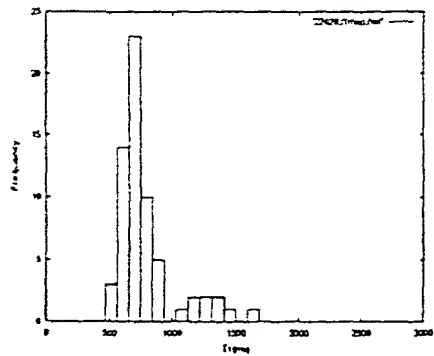
	
<p>C4. Histology of unoperated cartilage and bone</p> 	<p>C4 masks 2 and 4</p> 
<p>Histology of mask 2, cartilage</p>  <p>C4 masks 5 and 6</p>	<p>Histology of mask 4, bone</p>  <p>C4 masks 2 and 4</p>

Definition of masks 2, 4, 5, and 6 chosen for qMRI analysis of cartilage and bone.

C4 mask 2, unoperated cartilage

Parameter	Value	(s.e.)
M0(%)	48.8	0.5
T1(ms)	812	30
T2(ms)	12.8	0.5

Parameter	Value	(s.e.)
Msat/M0	0.116	0.007
T1sat(ms)	77	5
ADC(cm2/s)	8.1e-07	3.1e-07



Picg 3838-3843

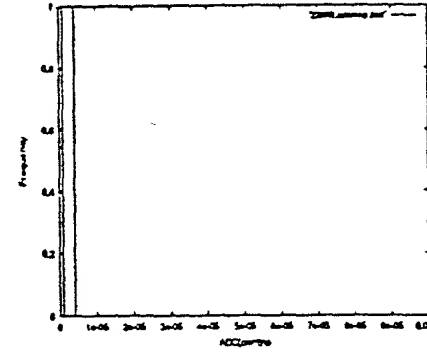
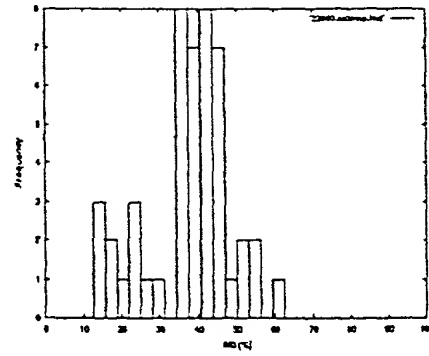
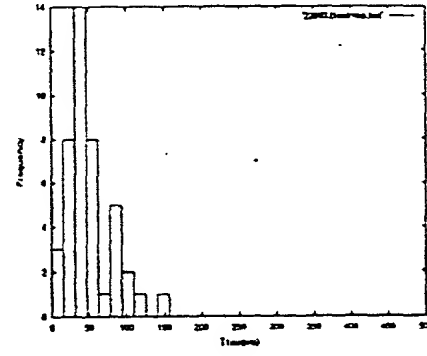
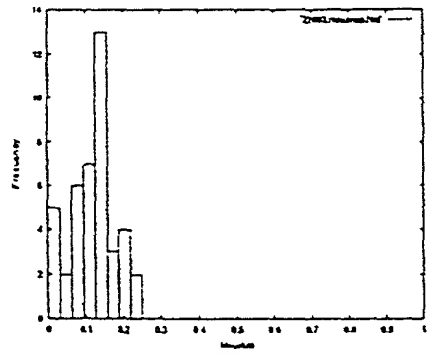
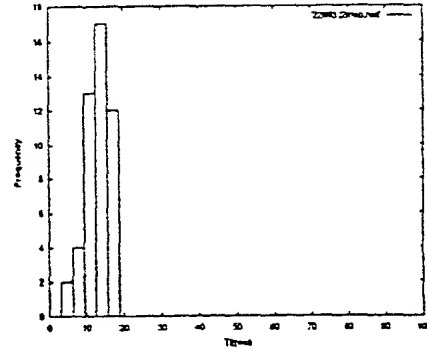
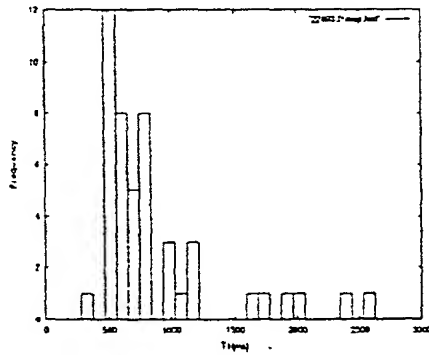
x axis - number of pixels with the same value
LHS- top T1, middle Msat/M0, bottom M0.

y axis - range of values.
RHS- top T2, mid T1sat, bottom ADC

Figure SRL 3. Automated output of histograms for C4 mask 2

C4 mask 5, unoperated cartilage

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	38.5	1.7	Msat/M0	0.125	0.009
T1(ms)	907	76	T1sat(ms)	53	5
T2(ms)	13.8	0.5	ADC(cm2/s)	6.4e-07	2.1e-07



Pic 3838-3843

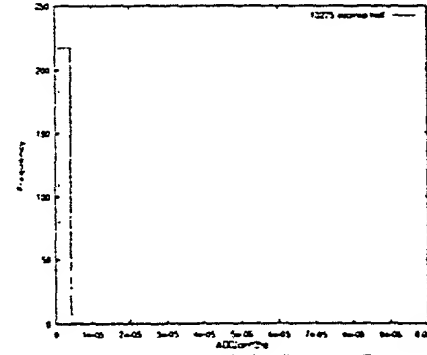
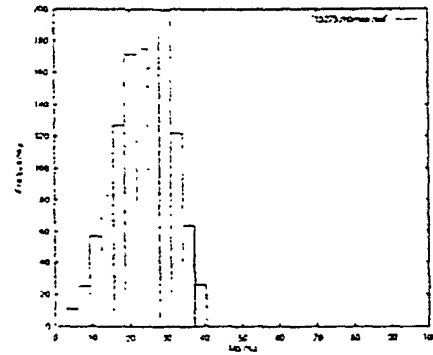
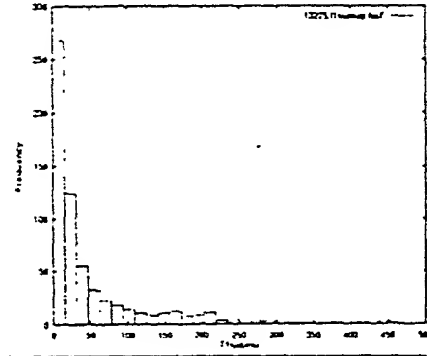
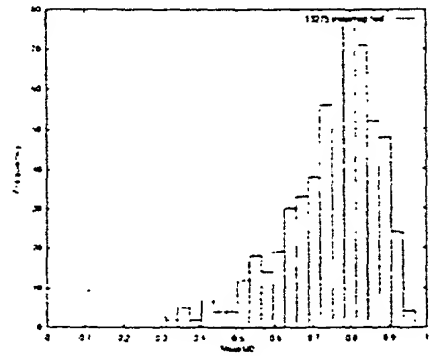
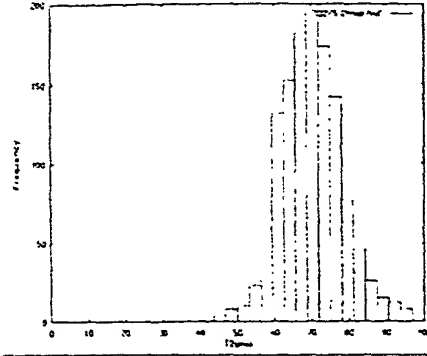
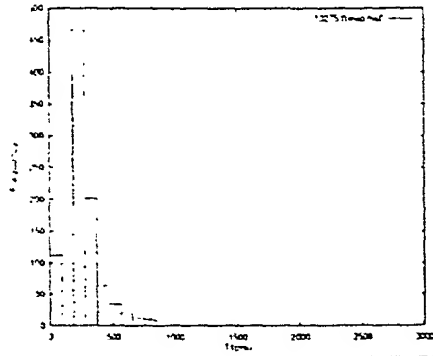
x axis – number of pixels with the same value
 LHS- top T1,middle Msat/M0, bottom M0.

y axis - range of values.
 RHS - top T2,mid T1sat,bottom ADC

Figure SRL 4 Automated output of histograms for C4 mask 5

C4 mask 4, unoperated bone

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	24.9	0.2	Msat/M0	0.769	0.006
T1(ms)	291	9	T1sat(ms)	63	4
T2(ms)	73.2	0.3	ADC(cm2/s)	8.6e-07	2.4e-08



Picg 3838-3843

x axis – number of pixels with the same value
 LHS- top T1, middle Msat/M0, bottom M0.

y axis - range of values.
 RHS - top T2, mid T1sat, bottom ADC

Figure SRL 5 Automated output of histograms for C4 mask 4.

C128 (ACD1 + HAED, vital flap) zero time point

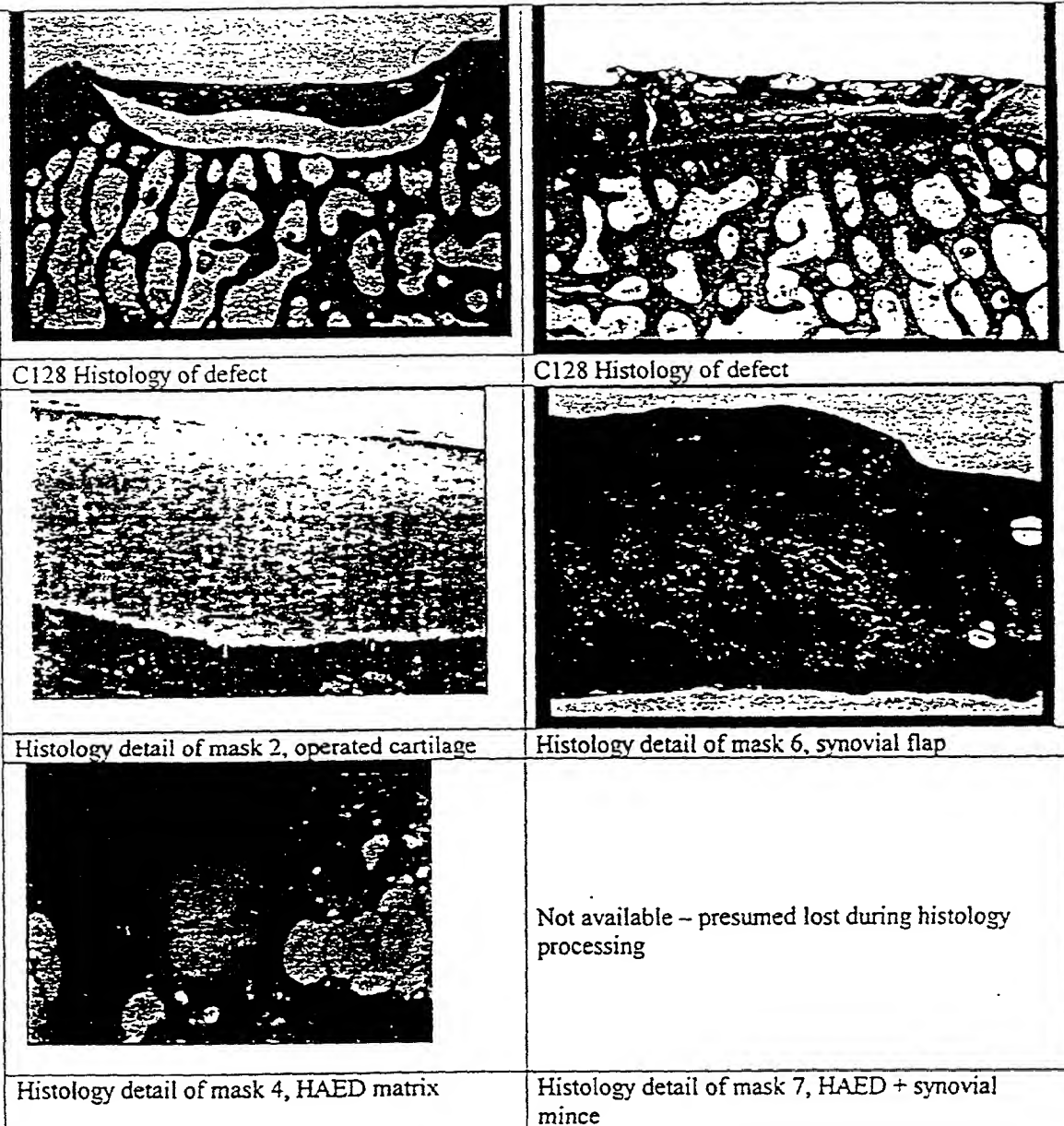
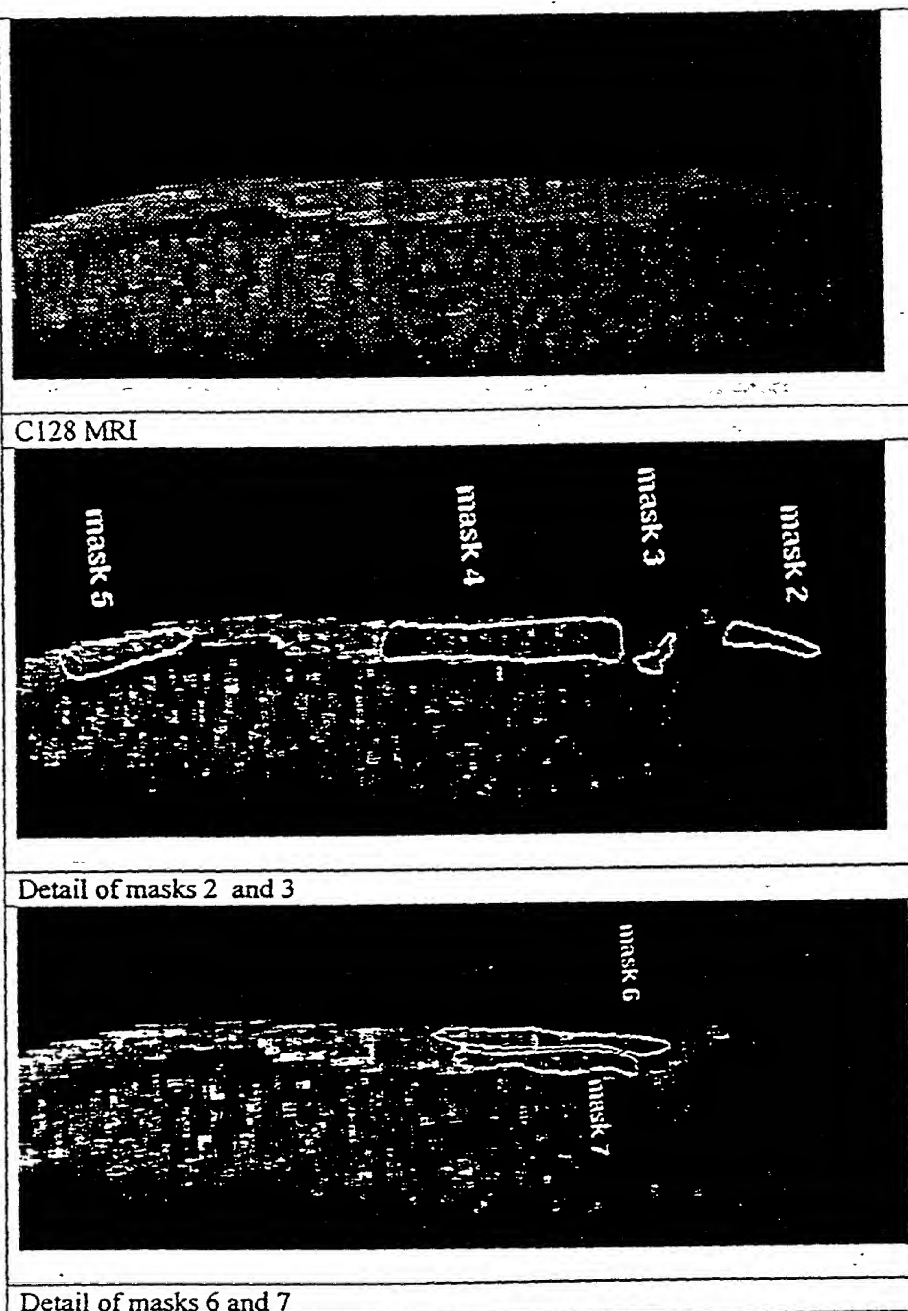


Figure SRL 6. C128 (ACD1 + HAED, vital flap) zero time point
 Histology showing detail of masks 2, 3, 6 and 7.

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qMRI analysis of C128



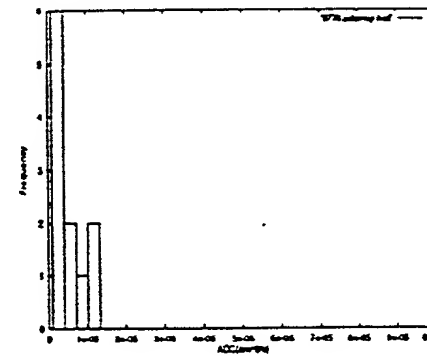
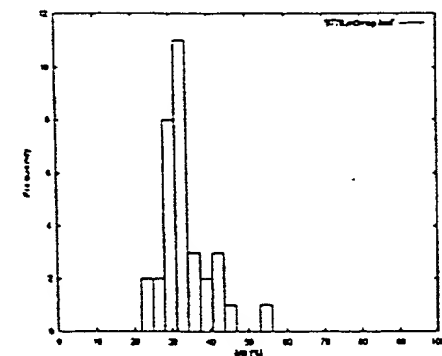
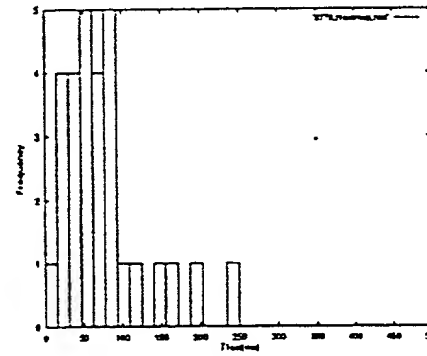
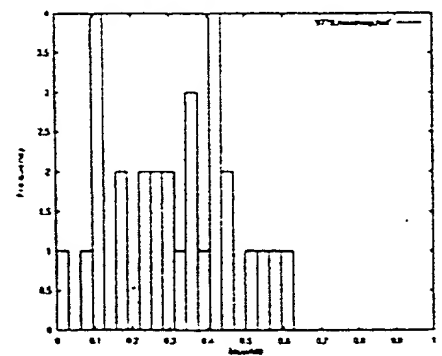
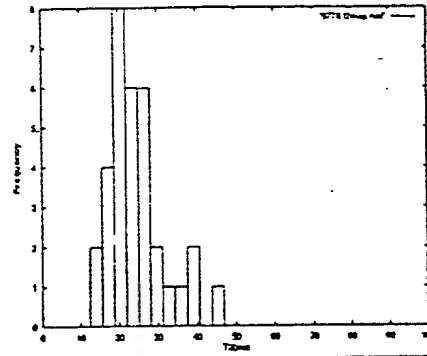
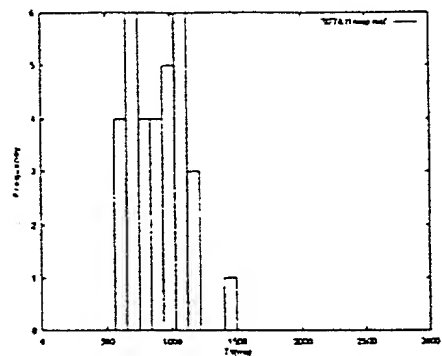
Detail of masks 6 and 7

Figure SRL 7. C128 (ACD1 + HAED, vital flap) zero time point
Definition of masks 2, 3, 6 and 7 for qMRI analysis.

09828070, 040501

C128 qMRI values for mask 2, cartilage adjacent to the defect

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	34.8	1.2	Msat/M0	0.326	0.031
T1(ms)	931	36	T1sat(ms)	79	10
T2(ms)	25.5	1.3	ADC(cm ² /s)	3.2e-06	9.4e-07



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x axis – number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

y axis - range of values.

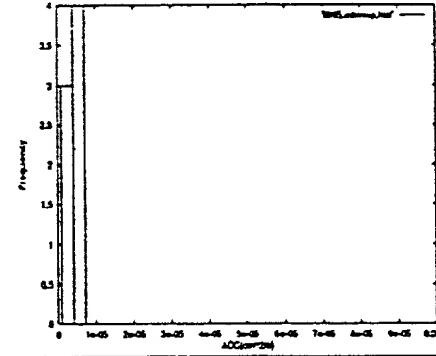
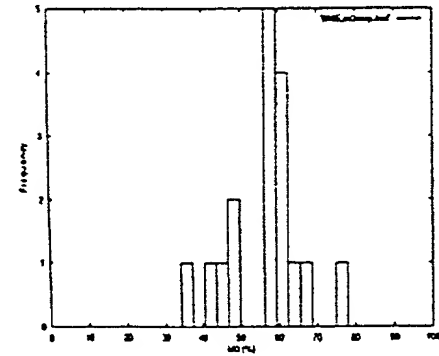
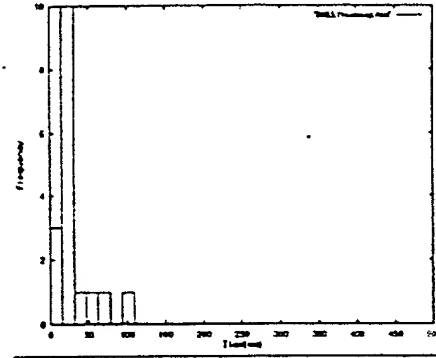
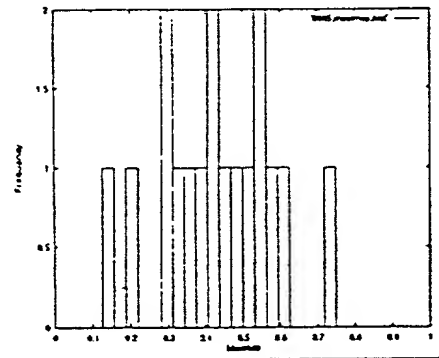
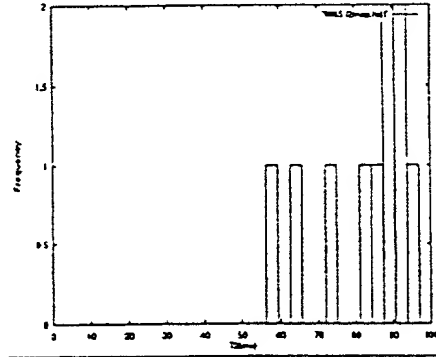
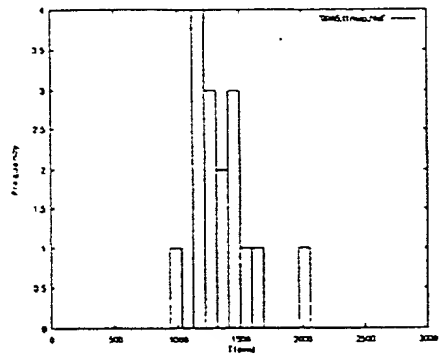
RHS top T2,mid T1sat,bottom ADC

Figure SRL 8. Automated output of histograms for C128 mask 2

C128 qMRI values for mask 3, HAED matrix

Parameter	Value	(s.e.)
M0(%)	58.5	2.5
T1(ms)	1684	200
T2(ms)	96.9	4.2

Parameter	Value	(s.e.)
Msat/M0	0.442	0.037
T1sat(ms)	31	6
ADC(cm ² /s)	3.4e-06	6.3e-07



ongg 493-498-3

x axis – number of pixels with the same value
LHS- top T1,middleMsat/M0,bottom M0.

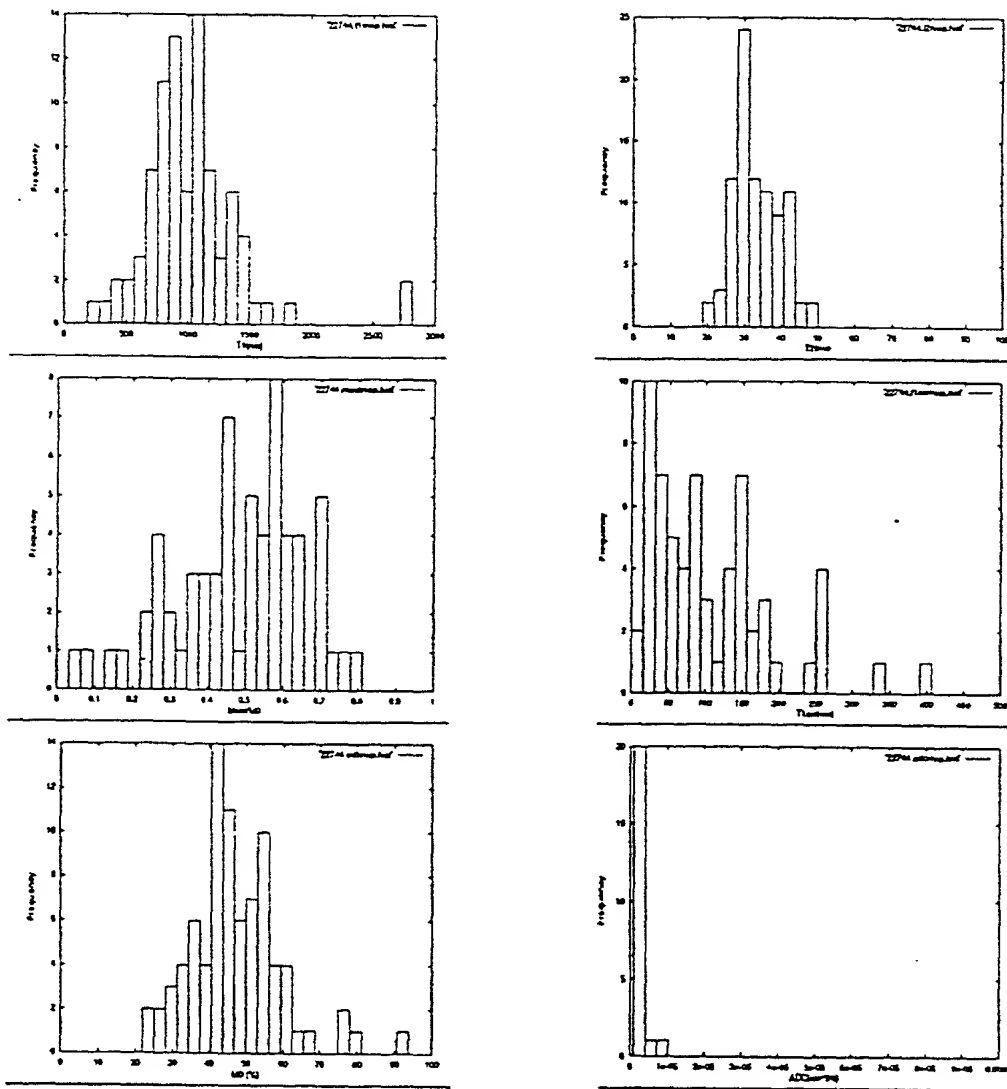
y axis - range of values.

RHS - top T2,mid T1sat,bottom ADC

Figure SRL 9. Automated output of histograms for C128 mask 3

C128 qMRI values for mask 6, synovial flap

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	48.7	1.4	Msat/M0	0.496	0.022
T1(ms)	1083	52	T1sat(ms)	110	11
T2(ms)	34.5	0.7	ADC(cm ² /s)	2e-06	3.2e-07



ongg 493-498-6

x axis - number of pixels with the same value
 LHS- top T1,middleMsat/M0,bottom M0.

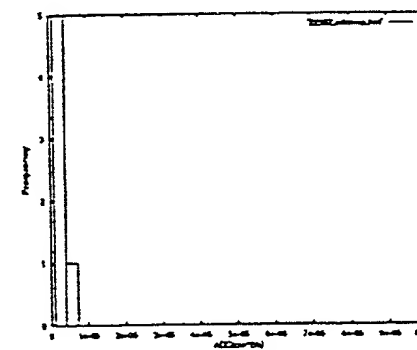
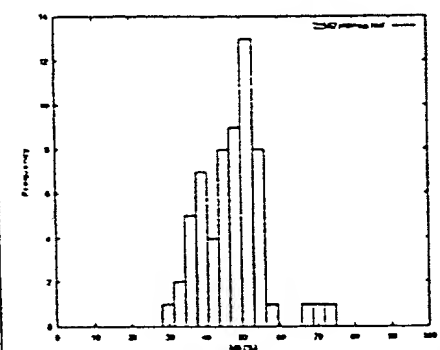
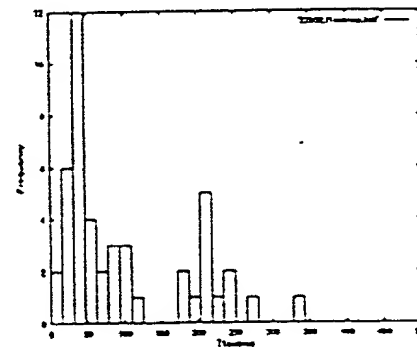
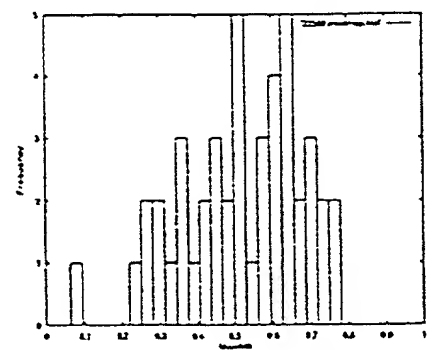
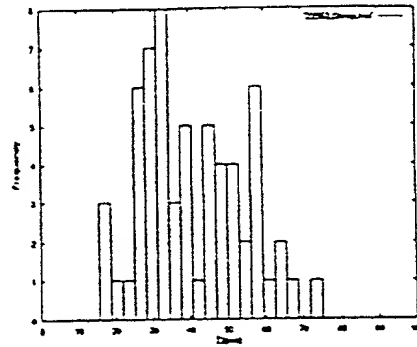
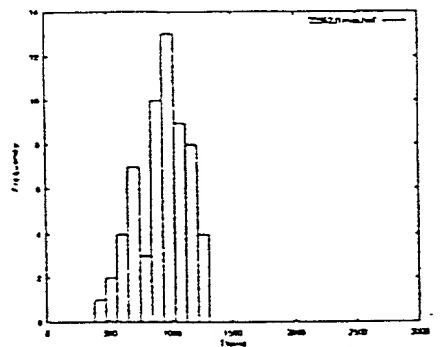
y axis - range of values.

RHS - top T2,mid T1sat,bottom ADC

Figure SRL 10. Automated output of histograms for C128 mask 6

C128 qMRI values for mask 7, HAED + synovial mince

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	49.0	1.1	Msat/M0	0.537	0.025
T1(ms)	968	27	T1sat(ms)	124	19
T2(ms)	42.2	1.8	ADC(cm ² /s)	2e-06	5.4e-07



ongg 493-498-7

x axis – number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

y axis - range of values.
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 11. Automated output of histograms for C128 mask 7

C129 (ACD1 + HAED, vital flap) 8 weeks

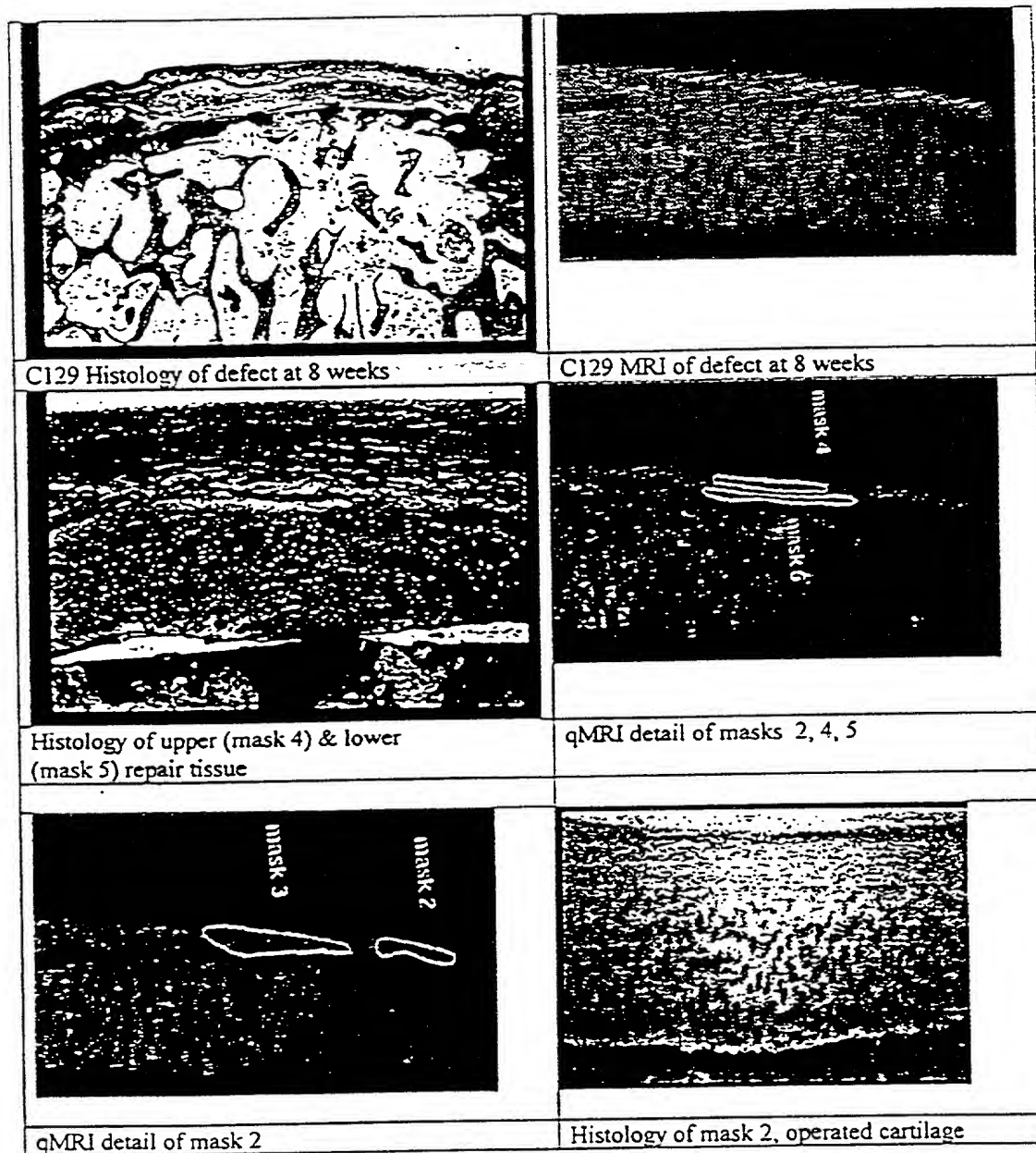


Figure SRL 12.

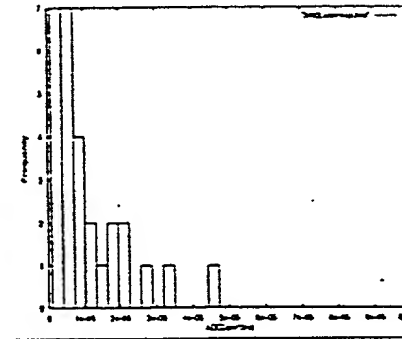
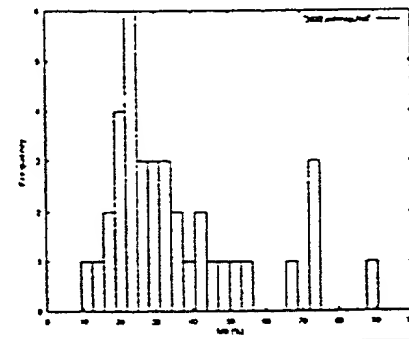
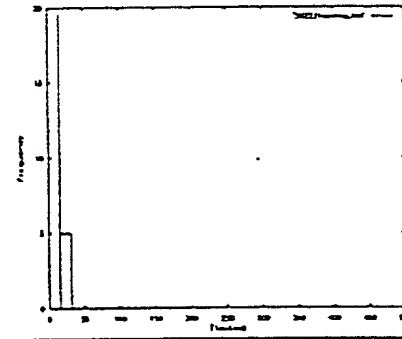
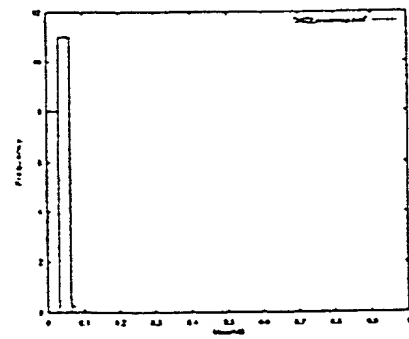
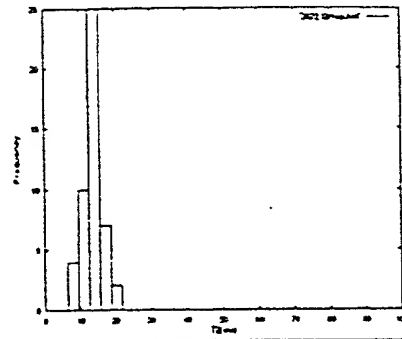
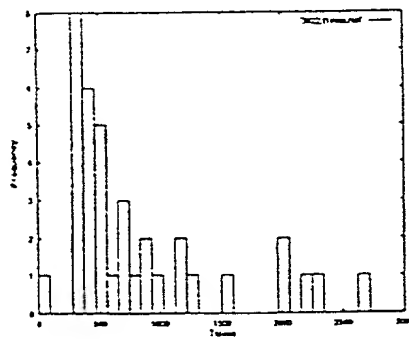
C129 (ACD1 + HAED, vital flap) 8 weeks

Histology and MRI showing detail of masks 2, 3, 4 and 5.

09828070-040504

C129 qMRI values for mask 2, cartilage adjacent to the defect

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	36.8	3.2	Msat/M0	0.032	0.003
T1(ms)	1092	173	T1sat(ms)	11	2
T2(ms)	14.2	0.4	ADC(cm ² /s)	1.1e-05	2e-06



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x axis – number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

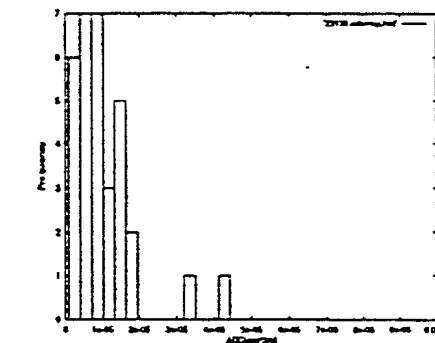
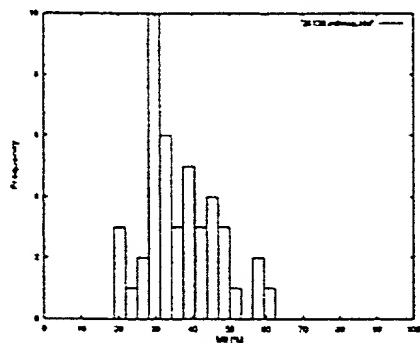
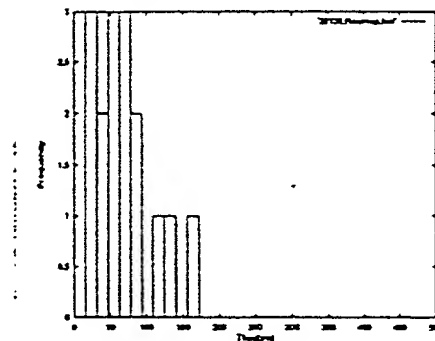
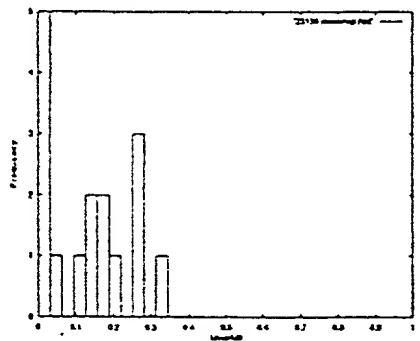
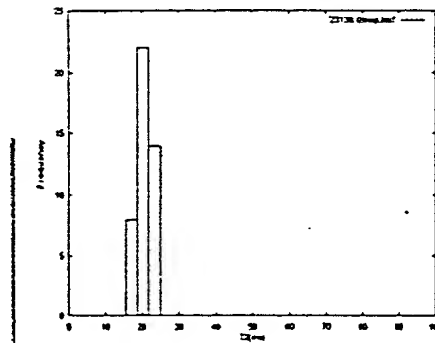
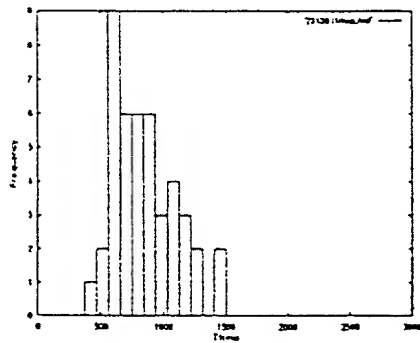
y axis - range of values.

RHS - top T2,mid T1sat,bottom ADC

Figure SRL 13. Automated output of histograms for C129 mask 2

C129 qMRI values for mask 5, lower repair tissue

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	38.0	1.6	Msat/M0	0.138	0.027
T1(ms)	876	40	T1sat(ms)	69	11
T2(ms)	21.8	0.3	ADC(cm2/s)	1e-05	1.5e-06



ongg752-757-5

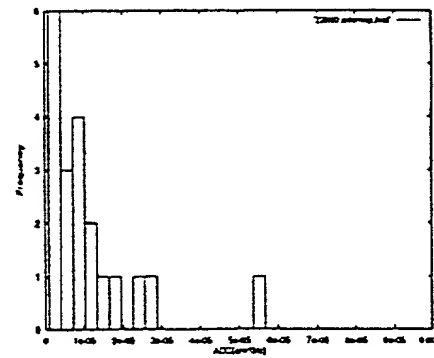
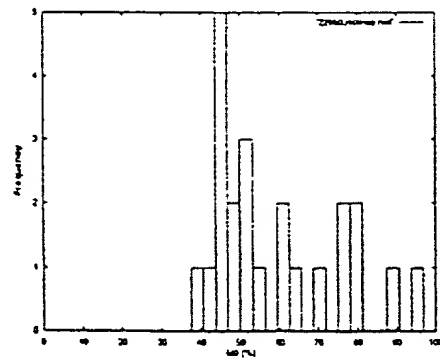
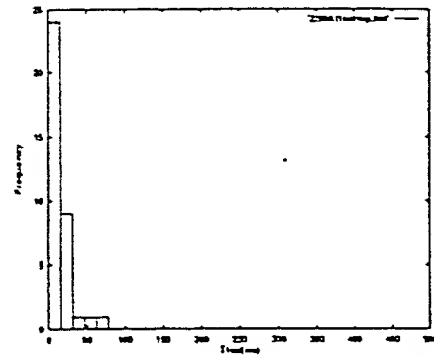
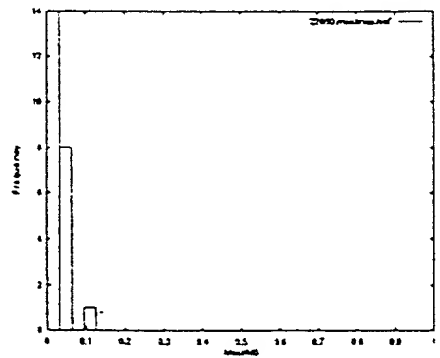
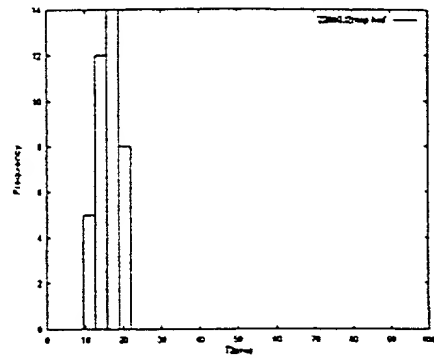
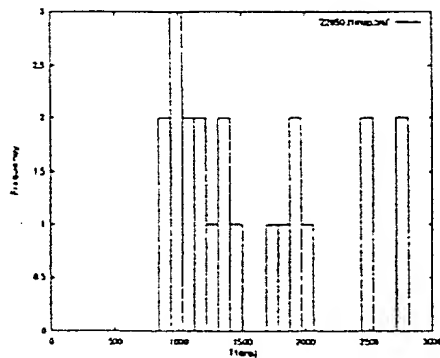
x axis – number of pixels with the same value
LHS- top T1,middleMsat/M0,bottom M0.

y axis - range of values.
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 14. Automated output of histograms for C129 mask 5

C129 qMRI values for mask 4, upper repair tissue

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	61.4	3.5	Msat/M0	0.036	0.005
T1(ms)	2025	227	T1sat(ms)	16	3
T2(ms)	16.8	0.4	ADC(cm2/s)	1.1e-05	2.7e-06



ongg752-757-4

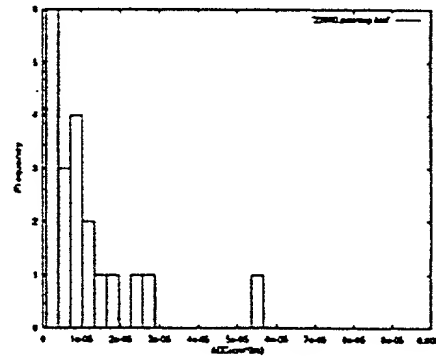
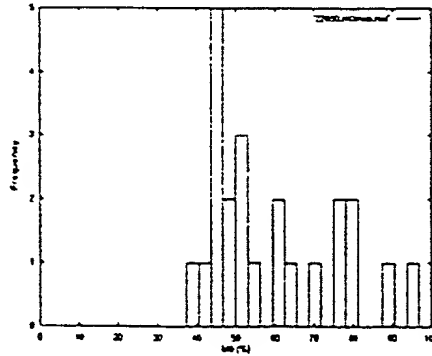
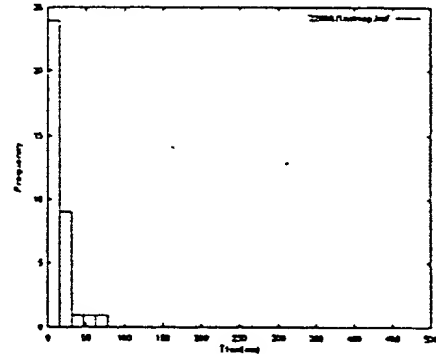
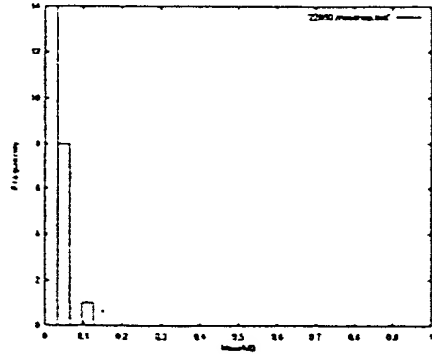
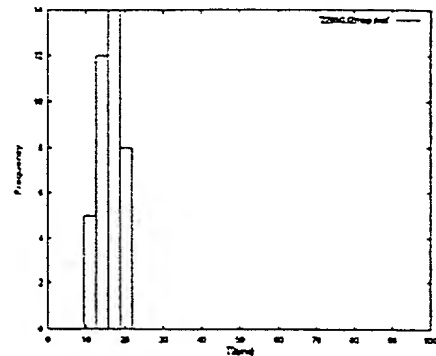
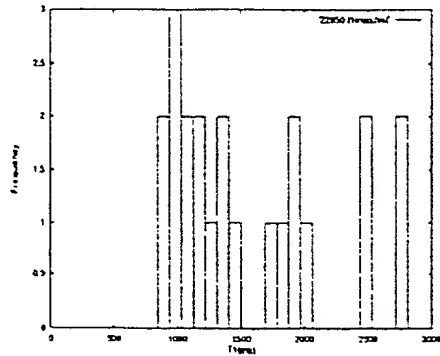
x axis – number of pixels with the same value
LHS- top T1, middle Msat/M0, bottom M0.

y axis - range of values.
RHS- top T2, mid T1sat, bottom ADC

Figure SRL 15. Automated output of histograms for C129 mask 4

C129 qMRI values for mask 3 repair tissue

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	61.4	3.5	Msat/M0	0.036	0.005
T1(ms)	2025	227	T1sat(ms)	16	3
T2(ms)	16.8	0.4	ADC(cm2/s)	1.1e-05	2.7e-06



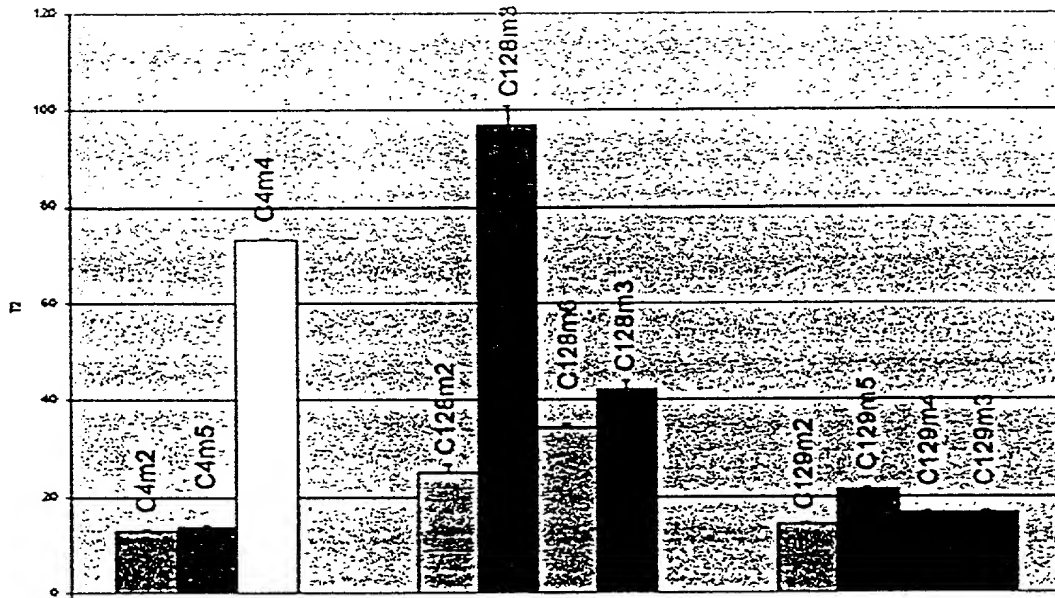
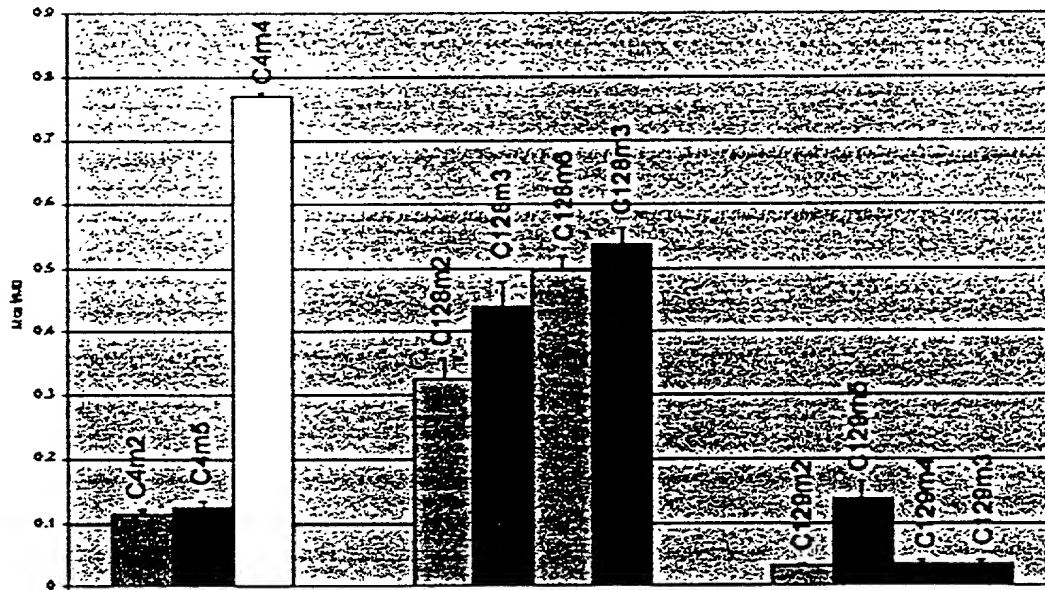
ongg752-757-3

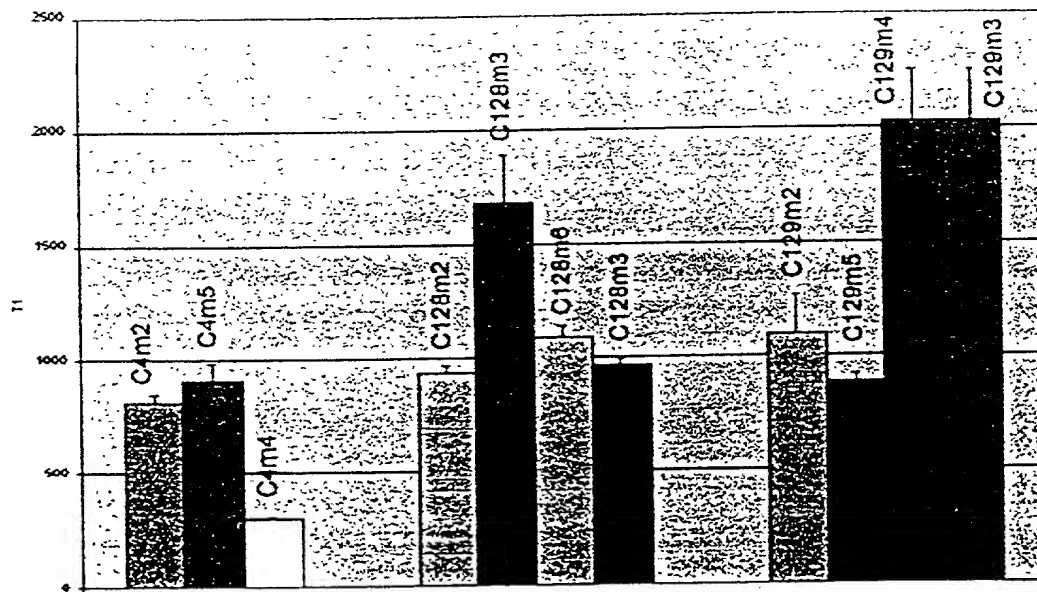
x axis – number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

y axis - range of values.

RHS - top T2,mid T1sat,bottom ADC

Figure SRL 16. Automated output of histograms for C129 mask 3

Comparison of T_2 and M_{sat}/M_0 cartilage, bone, matrix and synoviumFigure SRL 17a. Graphs comparing mean values of T_2 (above) and M_{sat}/M_0 (below) for ACD1 defects C128 and C129 with the unoperated control, C4



Comparison of T₁ and ADC for cartilage, bone, and synovium

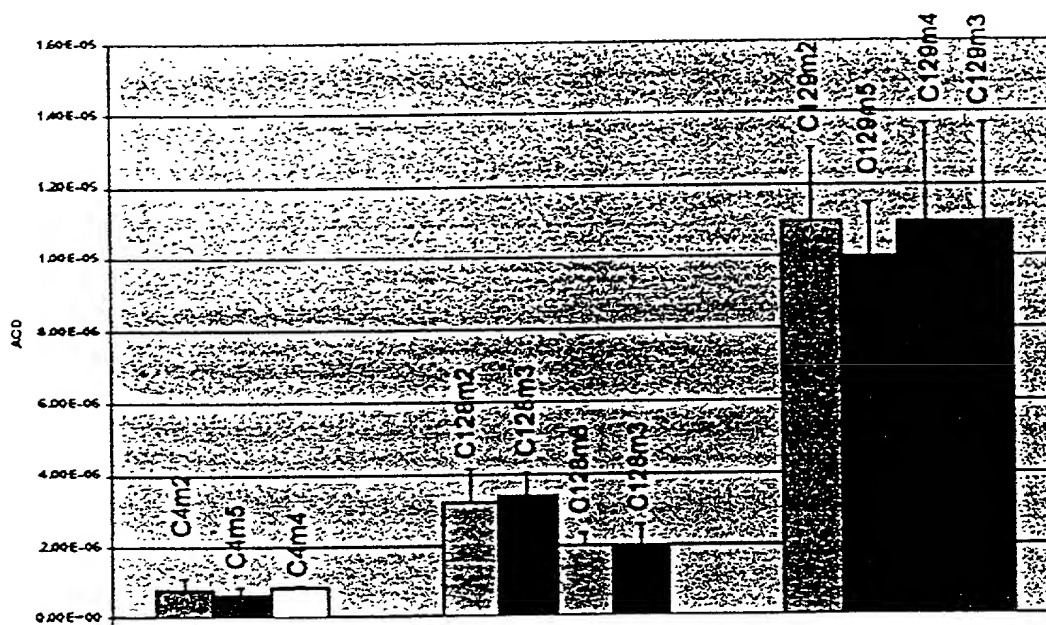


Figure SRL 17b. . Graphs comparing mean values of T₁ (above) and ADC (below) for ACD1 defects C128 and C129 with the unoperated control, C4

C146 (ACD1 - HAED, vital flap) 8 weeks

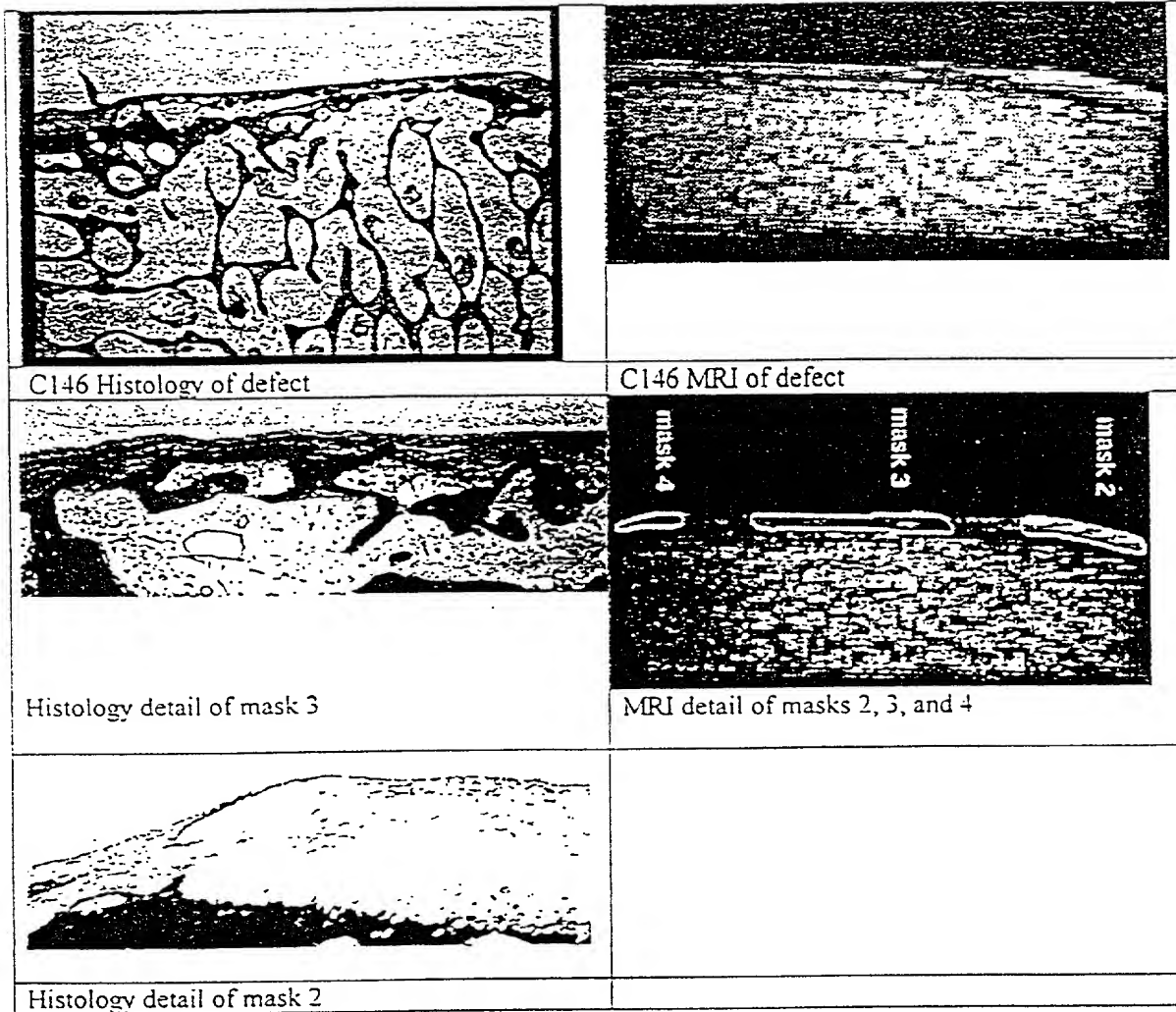


Figure SRL 18

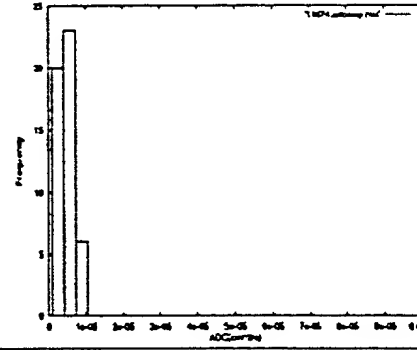
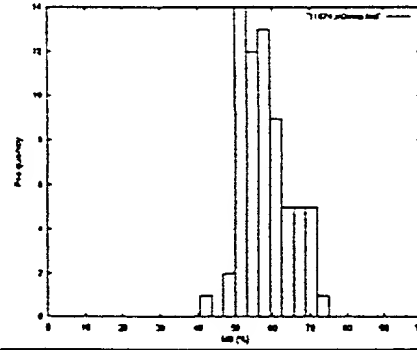
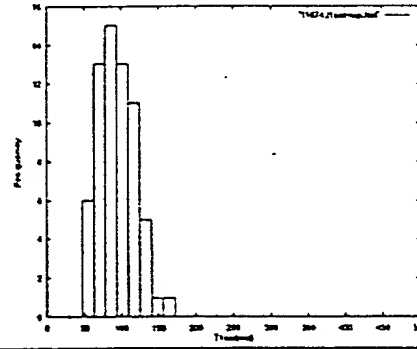
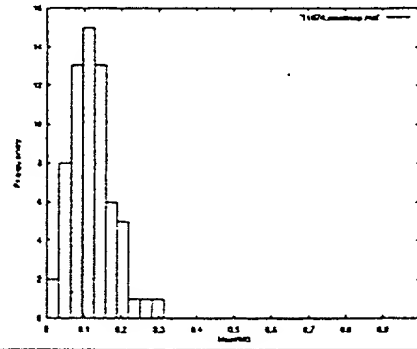
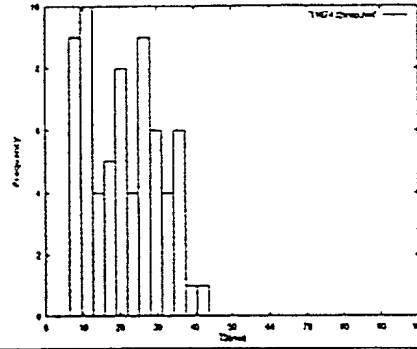
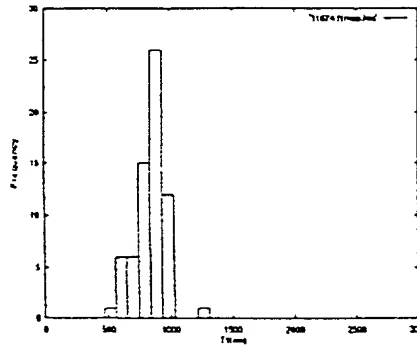
C146 (ACD1 + HAED, vital flap) 8 weeks

Histology and MRI showing detail of masks 2, 3 and 4.

09828070 044501

C146 qMRI values for mask 2, adjacent cartilage

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	60.0	0.8	Msat/M0	0.124	0.007
T1(ms)	873	15	T1sat(ms)	97	3
T2(ms)	22.1	1.2	ADC(cm2/s)	4.3e-06	3.4e-07



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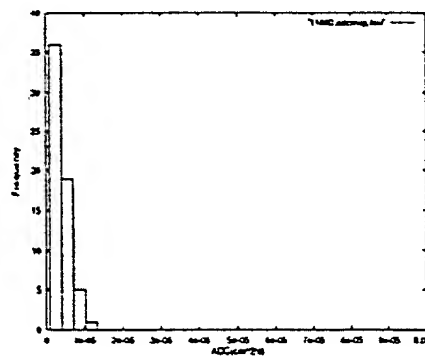
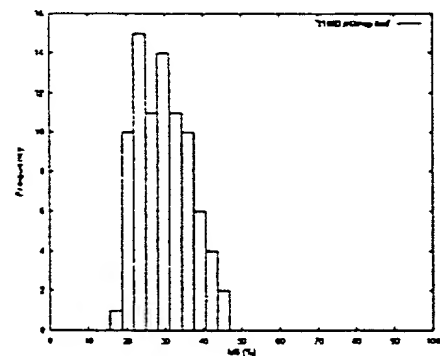
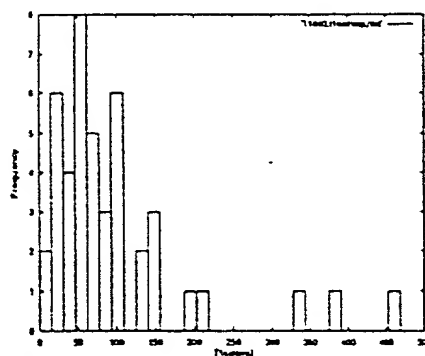
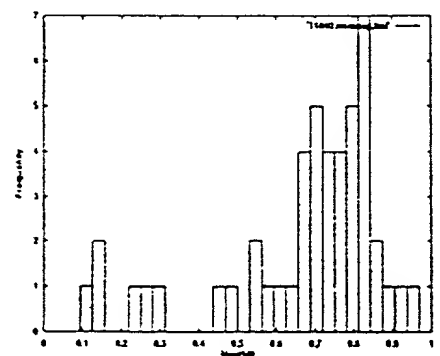
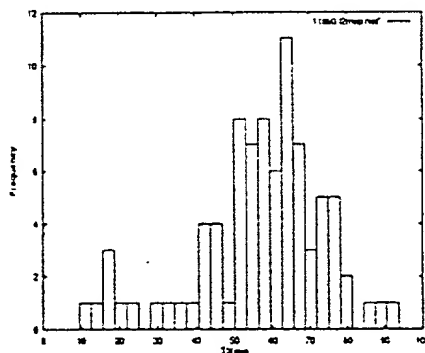
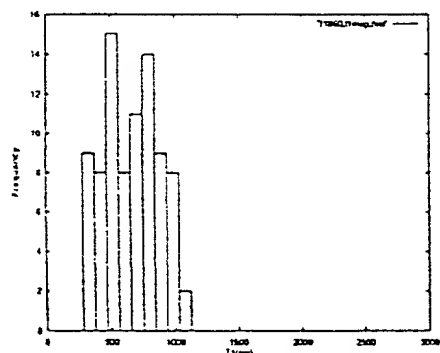
x axis – number of pixels with the same value
LHS- top T1, middle Msat/M0, bottom M0.y axis - range of values.
RHS - top T2, mid T1sat, bottom ADC

Figure SRL 19. Automated output of histograms for C146 mask 2

C146 qMRI values for mask 3, repair tissue

Parameter	Value	(s.e.)
M0(%)	30.6	0.8
T1(ms)	688	24
T2(ms)	58.9	1.9

Parameter	Value	(s.e.)
Msat/M0	0.692	0.032
T1sat(ms)	119	19
ADC(cm ² /s)	3.6e-06	3e-07



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x axis – number of pixels with the same value

y axis - range of values.

LHS- top T1,middleMsat/M0,bottom M0.

RHS- top T2,mid T1sat,bottom ADC

Figure SRL 20. Automated output of histograms for C146 mask 3

C131 (ACD1 - HAED, partially devitalised flap) 6 weeks

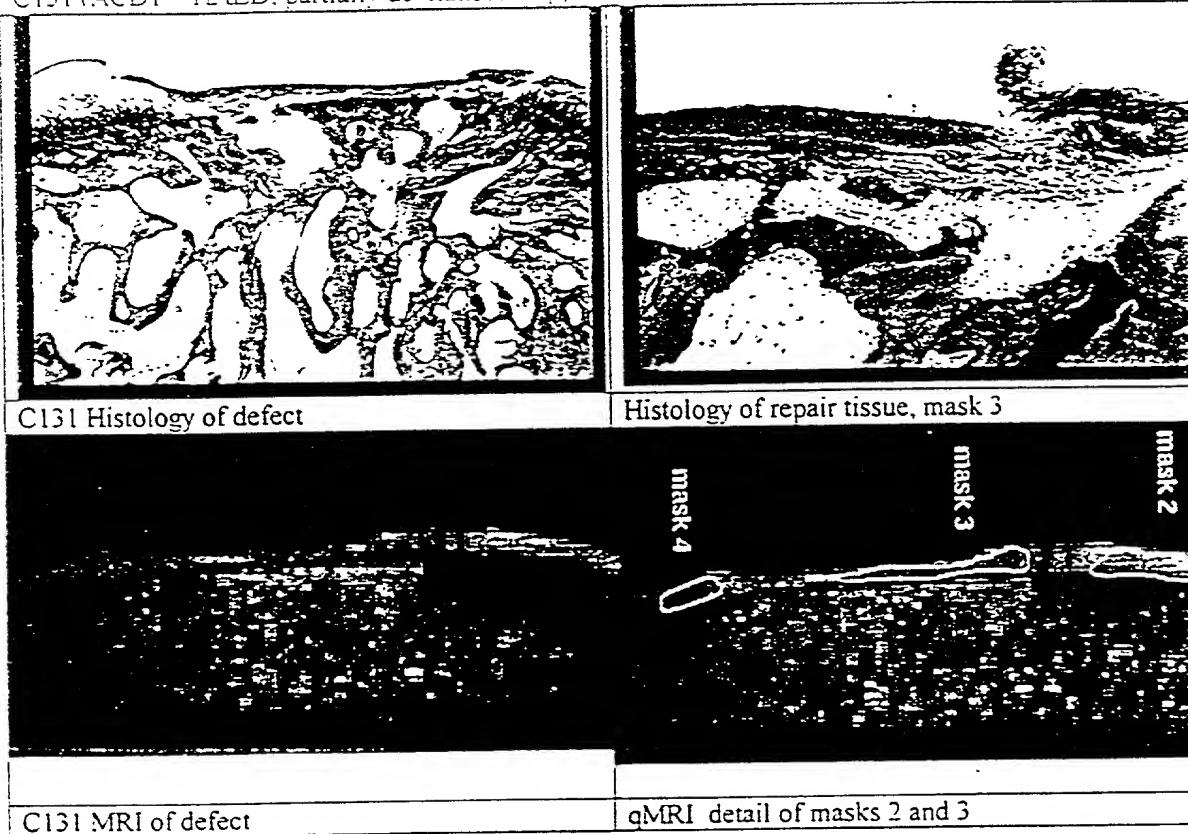


Figure SRL 21

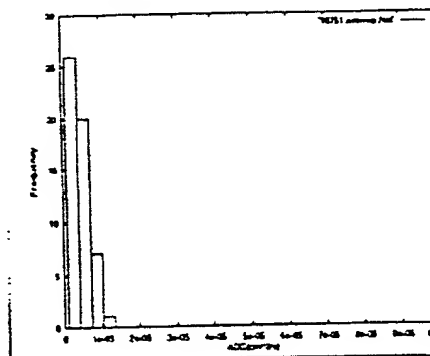
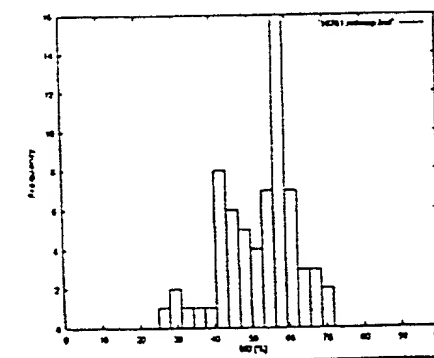
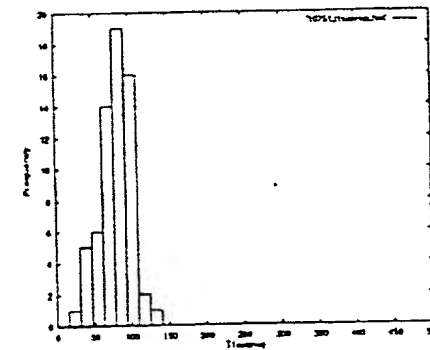
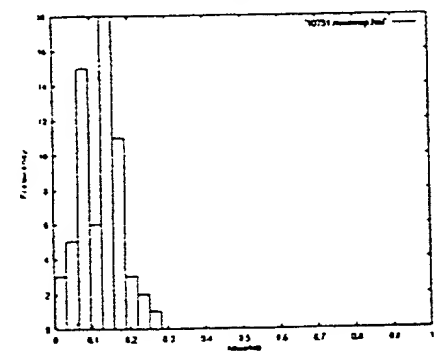
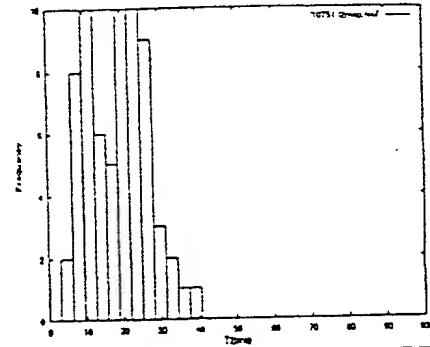
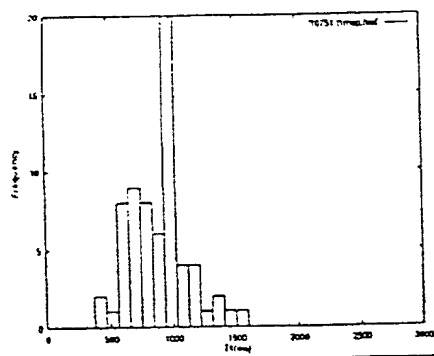
C131 (ACD1 - HAED, partially devitalised flap) 6 weeks

Histology and MRI showing detail of masks 2 and 3.

09828070.040501

C131 qMRI values for mask 2, cartilage adjacent to the defect

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	54.2	1.2	Msat/M0	0.129	0.007
T1(ms)	930	29	T1sat(ms)	84	3
T2(ms)	19.8	1.0	ADC(cm2/s)	4.3e-06	3.3e-07



ongg-598-603-2

x axis – number of pixels with the same value
LHS- top T1,middleMsat/M0,bottom M0.

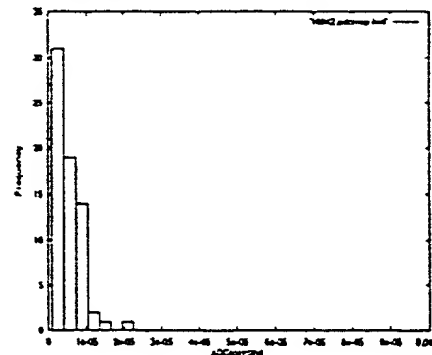
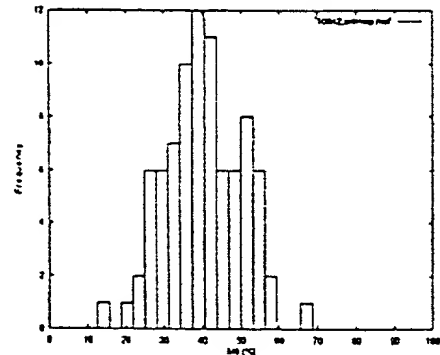
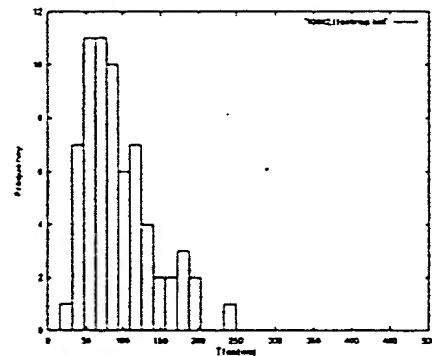
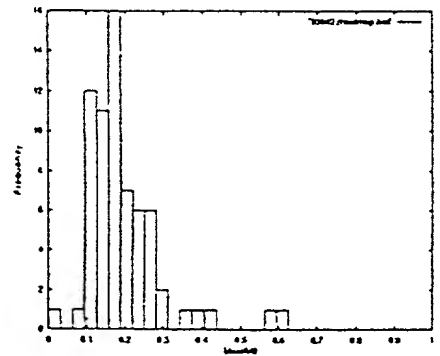
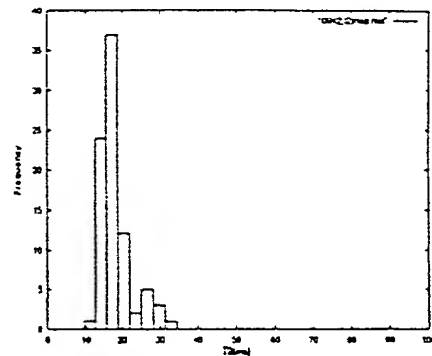
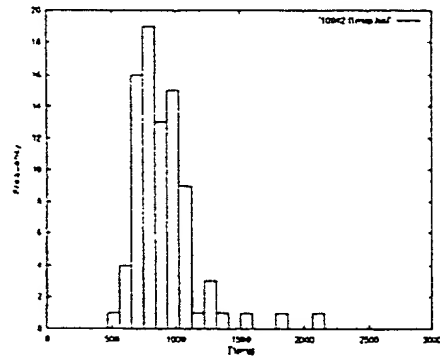
y axis - range of values.
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 22. Automated output of histograms for C131 mask 2

C131 qMRI values for mask 3, repair tissue

Parameter	Value	(s.e.)
M0(%)	41.7	1.1
T1(ms)	936	28
T2(ms)	18.6	0.5

Parameter	Value	(s.e.)
Msat/M0	0.202	0.013
T1sat(ms)	97	6
ADC(cm ² /s)	5.3e-06	4.3e-07



ongg 598-603-3

x axis – number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

y axis - range of values.

RHS - top T2,mid T1 sat,bottom ADC

Figure SRL 23. Automated output of histograms for C131 mask 3

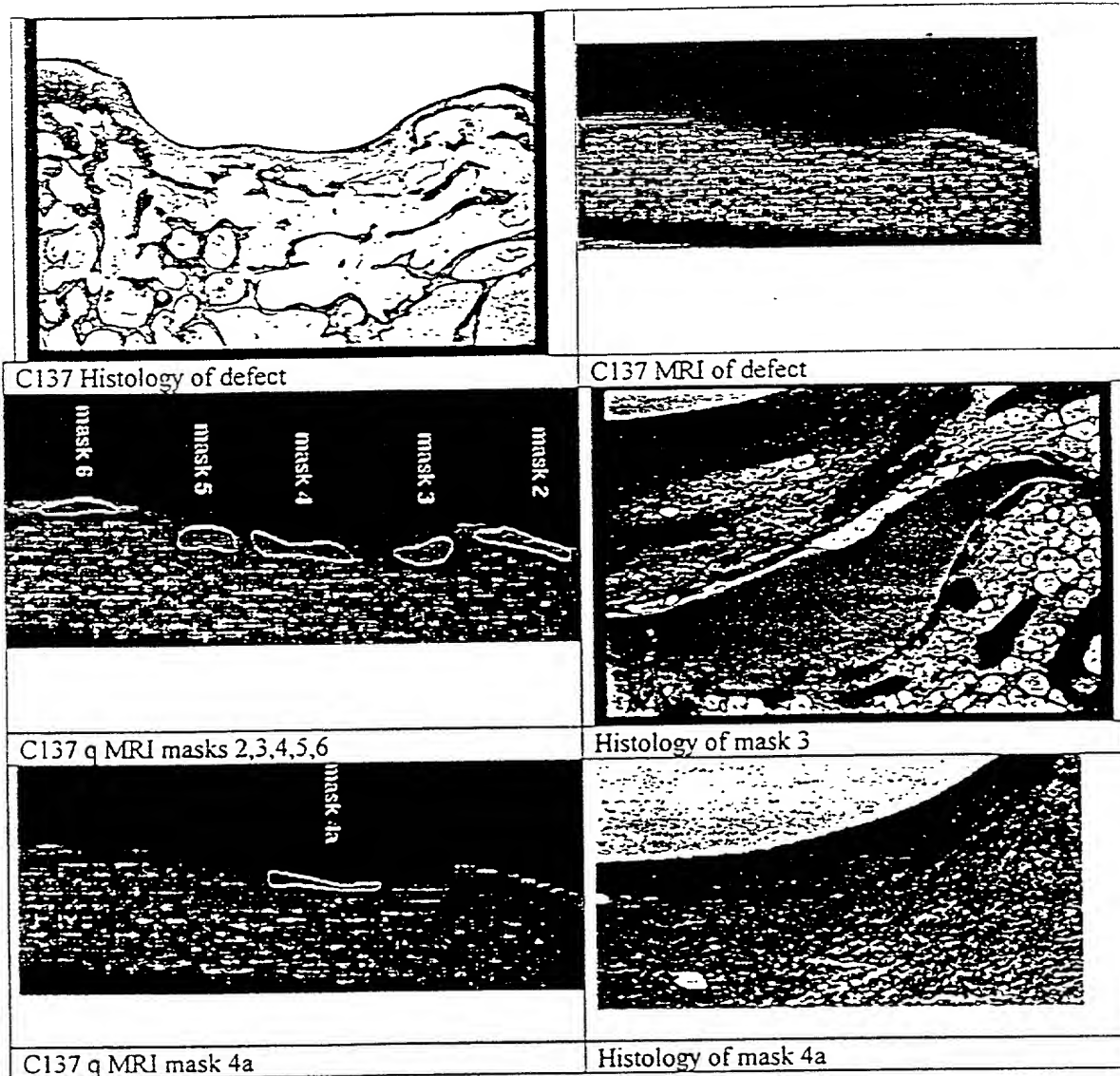


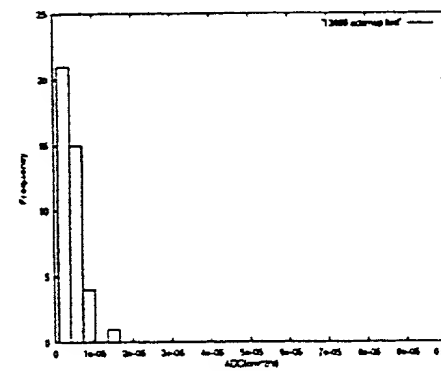
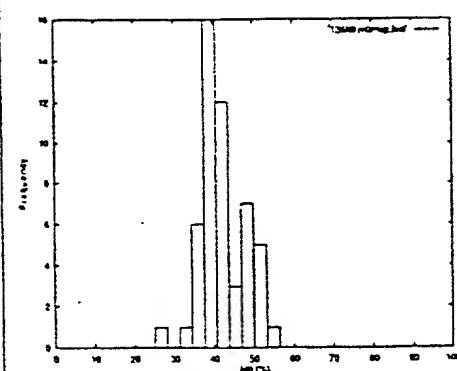
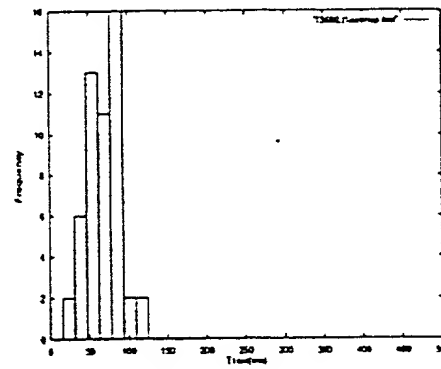
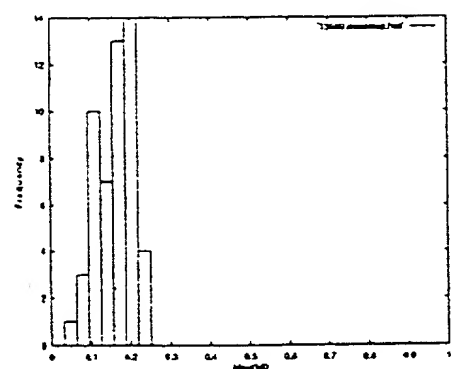
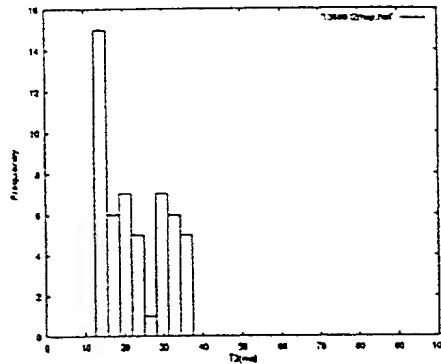
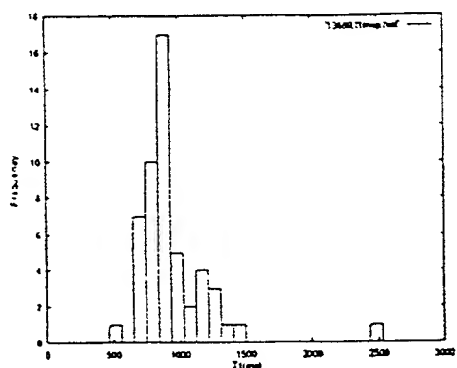
Figure SRL 24.

C137 (virtual ACD1 + PEG Triacrylate, partially devitalised flap) 10 weeks
 Histology and MRI showing detail of masks 2, 3, 4, 4a, 5 and 6.

C137 mask 2, cartilage adjacent to the defect

Parameter	Value	(s.e.)
M0(%)	43.6	0.8
T1(ms)	982	40
T2(ms)	23.6	1.1

Parameter	Value	(s.e.)
Msat/M0	0.167	0.007
T1sat(ms)	72	3
ADC(cm ² /s)	4.3e-06	4.2e-07



ongg 941-946-2

x axis - number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

y axis - range of values.

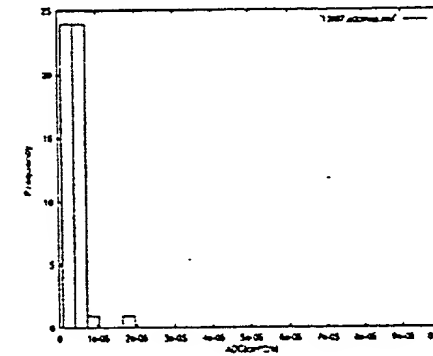
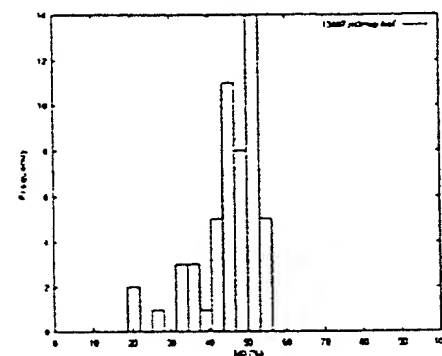
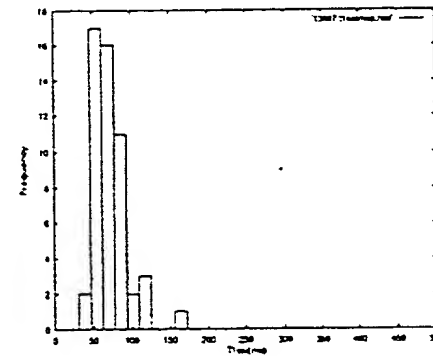
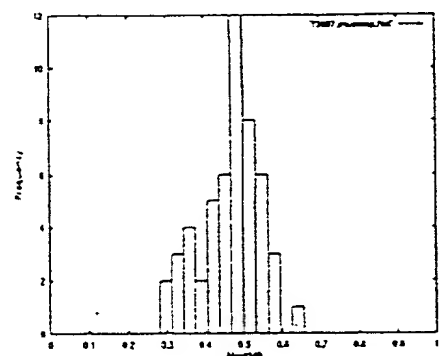
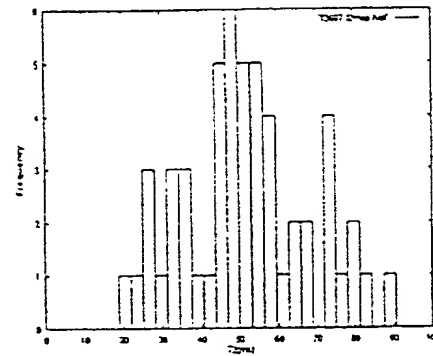
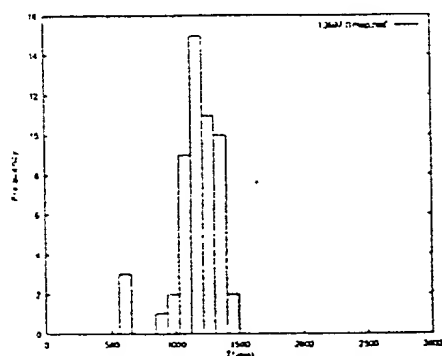
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 25. Automated output of histograms for C137 mask 2

C137 mask 3, retained matrix

Parameter	Value	(s.e.)
M0(%)	46.8	1.1
T1(ms)	1219	26
T2(ms)	53.4	2.3

Parameter	Value	(s.e.)
Msat/M0	0.480	0.011
T1sat(ms)	75	3
ADC(cm2/s)	4.5e-06	3.7e-07



ongg 941-946-3

x axis – number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

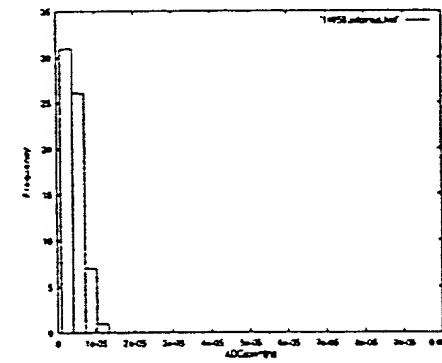
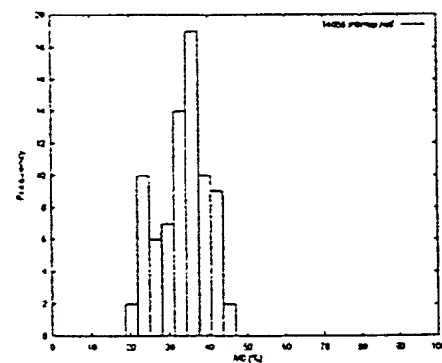
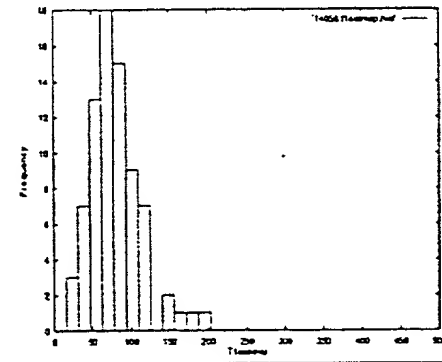
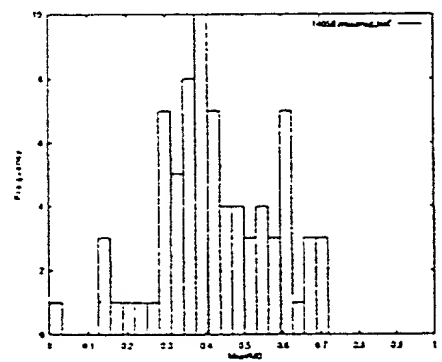
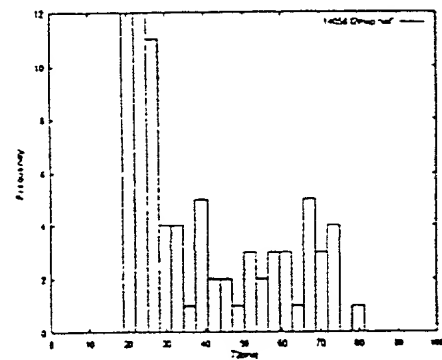
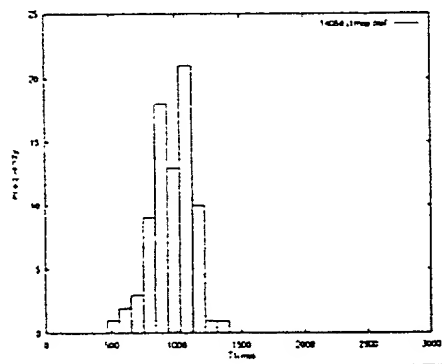
y axis - range of values.
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 26. Automated output of histograms for C137 mask 3

C137 mask 4, lower repair tissue

Parameter	Value	(s.e.)
M0(%)	34.8	0.7
T1(ms)	1009	18
T2(ms)	40.9	2.2

Parameter	Value	(s.e.)
Msat/M0	0.443	0.017
T1sat(ms)	83	4
ADC(cm2/s)	4.4e-06	3e-07



ongg 941-946-4

x axis – number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

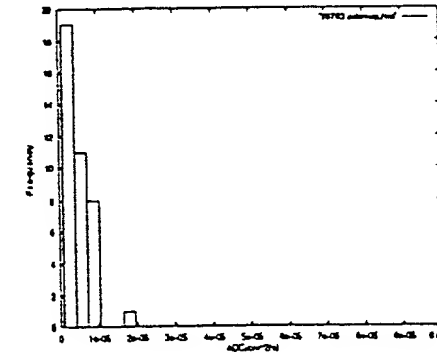
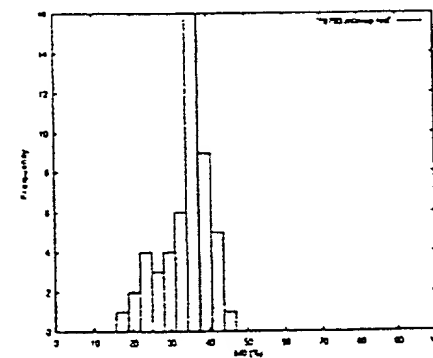
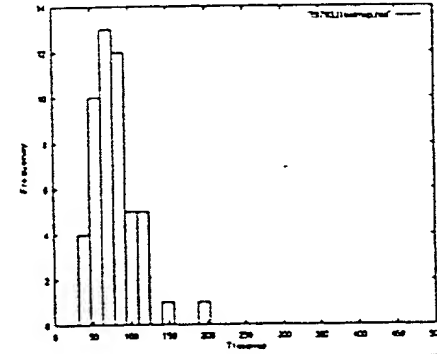
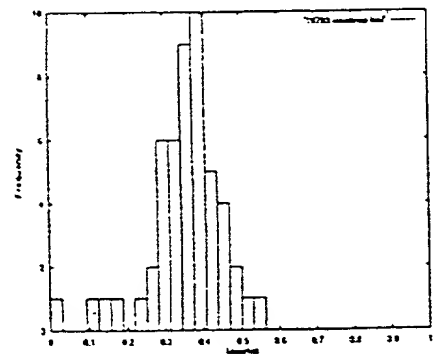
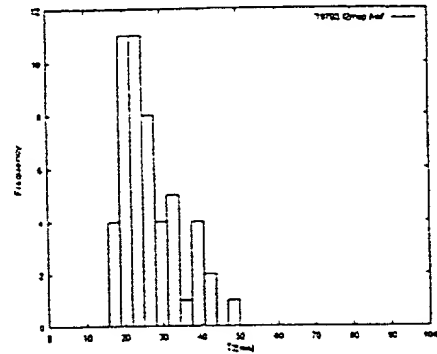
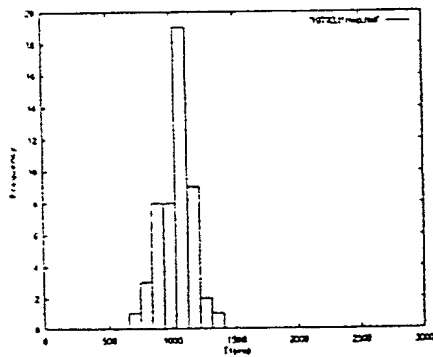
y axis - range of values.
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 27. Automated output of histograms for C137 mask 4

C137 mask 4a, upper repair tissue

Parameter	Value	(s.e.)
M0(%)	35.4	0.9
T1(ms)	1080	19
T2(ms)	27.7	1.1

Parameter	Value	(s.e.)
Msat/M0	0.365	0.014
T1sat(ms)	83	4
ADC(cm2/s)	5e-06	5.2e-07



ongg 941-946-4a

x axis - number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

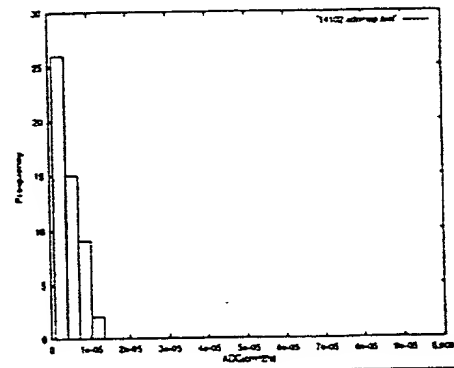
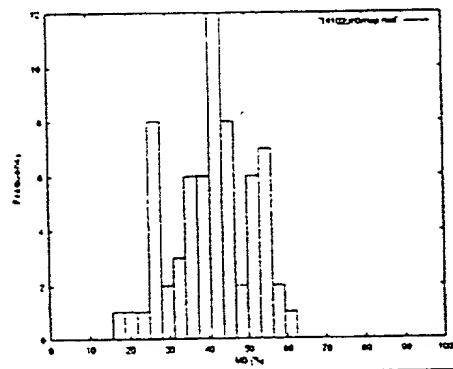
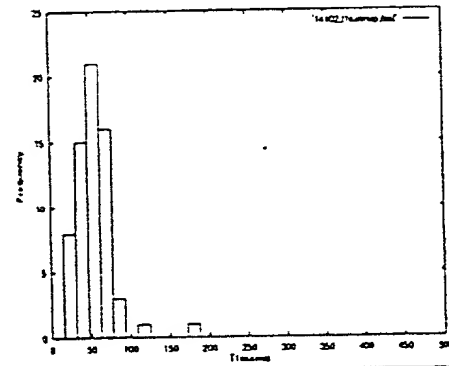
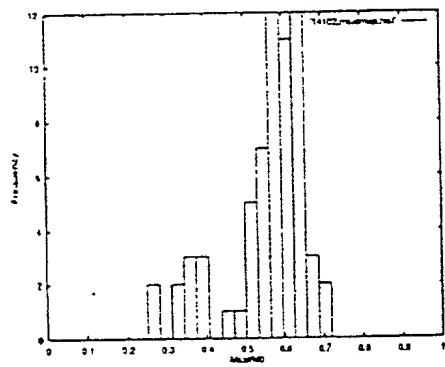
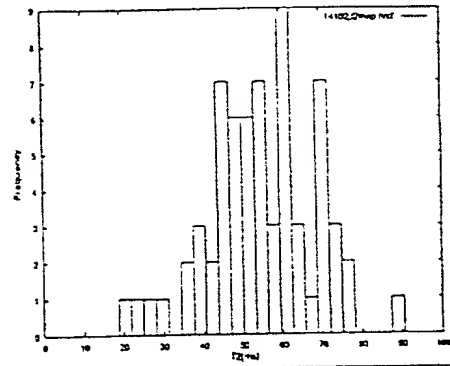
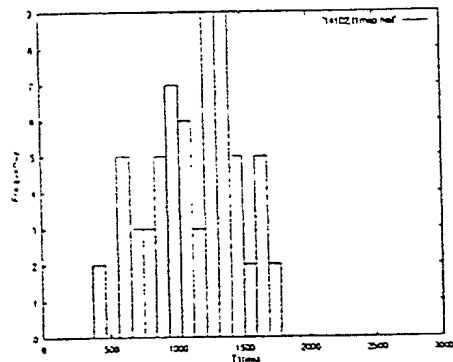
y axis - range of values.
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 28. Automated output of histograms for C137 mask 4a

C137 mask 5. retained matrix

Parameter	Value	(s.e.)
M0(%)	42.7	1.3
T1(ms)	1173	42
T2(ms)	56.4	1.7

Parameter	Value	(s.e.)
Msat/M0	0.576	0.014
T1sat(ms)	57	3
ADC(cm2/s)	4.5e-06	3.7e-07



ongg 941-946-5

x axis - number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

y axis - range of values.

RHS - top T2,mid T1sat,bottom ADC

Figure SRL 29. Automated output of histograms for C137 mask 5

qMRI analysis of repair tissue in ACD3 defects

















	C2	C1	C79	C78
T2 relaxation (1 st echo) TR 1500ms TE 6ms				
T2 relaxation (last echo) TR 1500ms TE 48ms				
T1 relaxation TR 500ms TE 6ms				
MT contrast 200ms saturation				

Figure SRL 30.

Selected MR scans from qMRI analysis of spontaneously healed ACD3 defects
C1, C2 at 8 weeks and C78, C79 at 6 months.

FO5040" 04082860

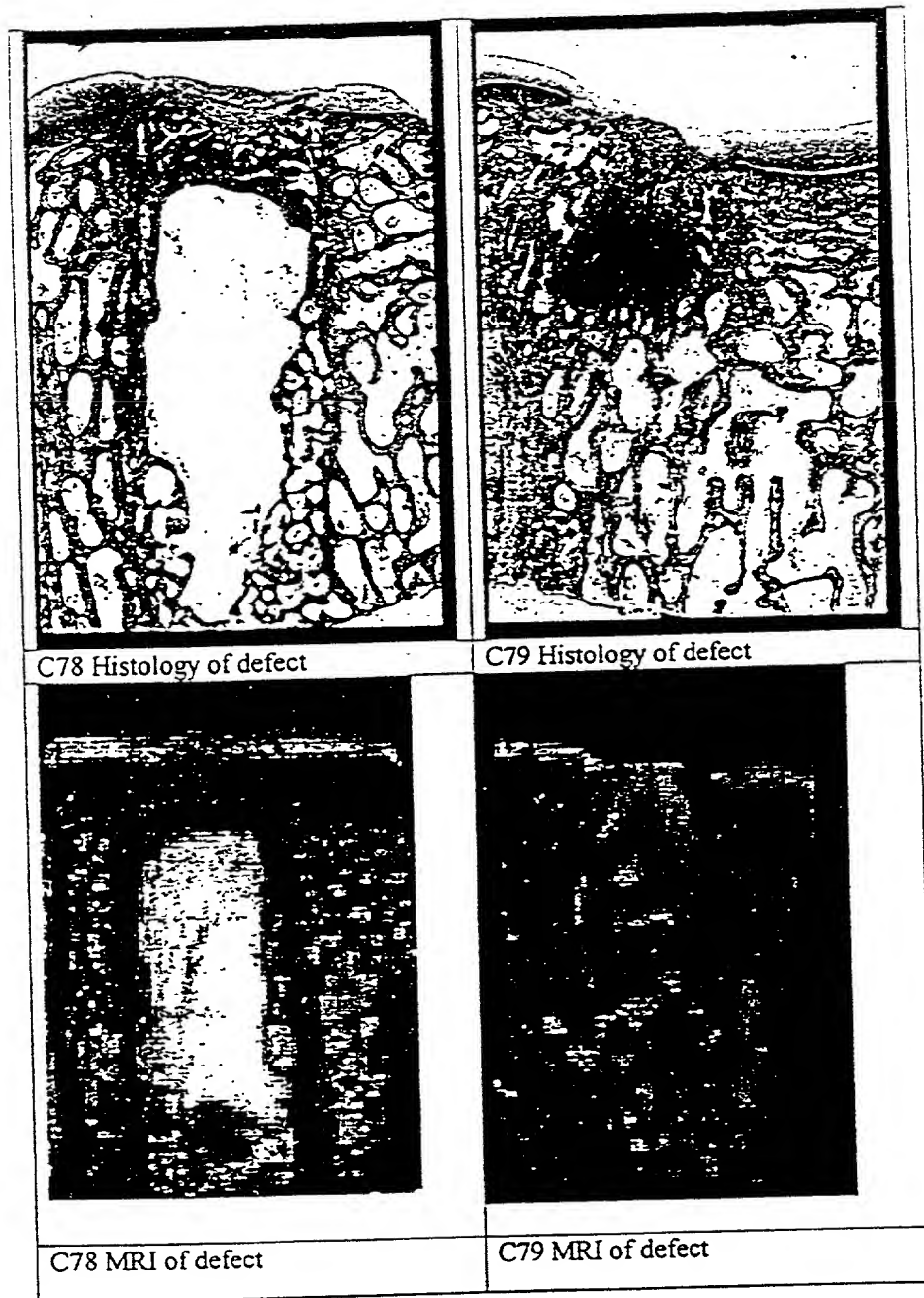


Figure SRL 31

Histology and MRI of spontaneously healed ACD3 defects C78 and C79 at 6 months

09220070 04501

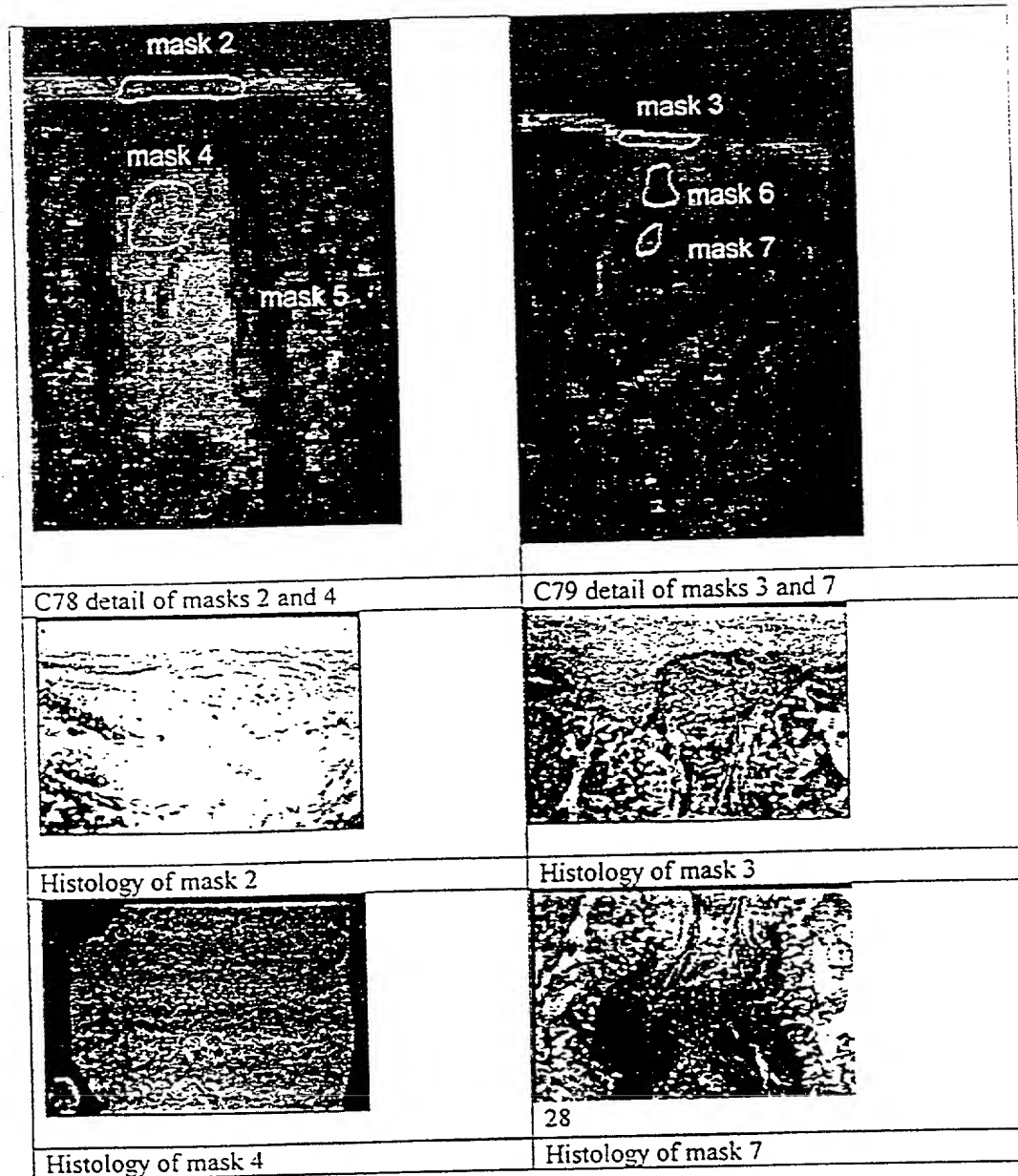


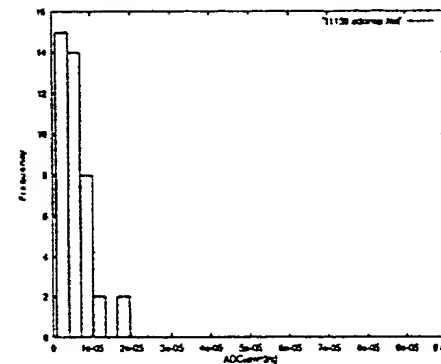
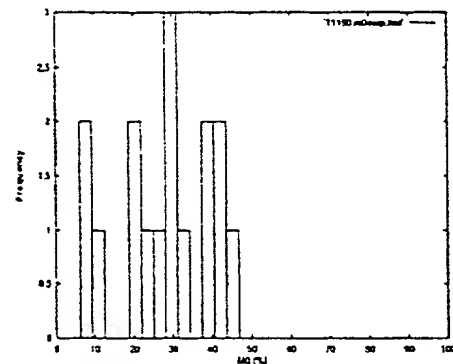
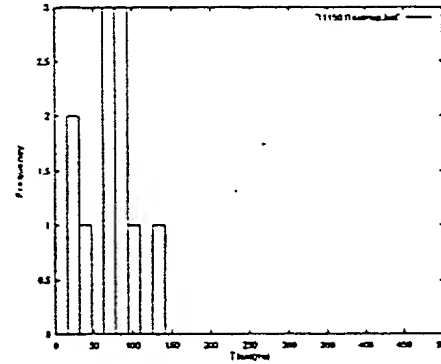
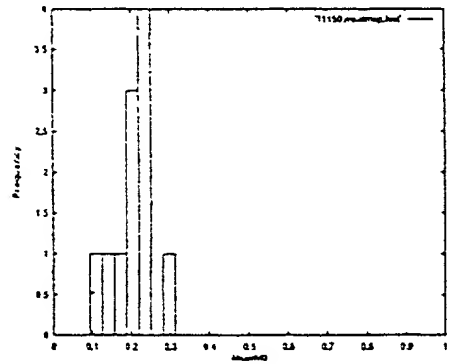
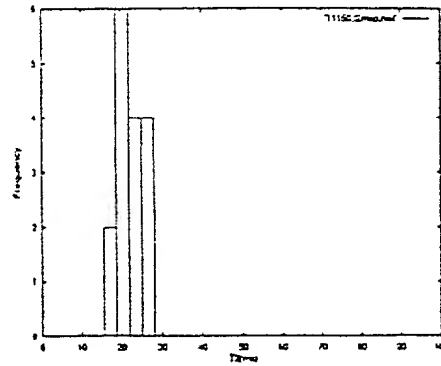
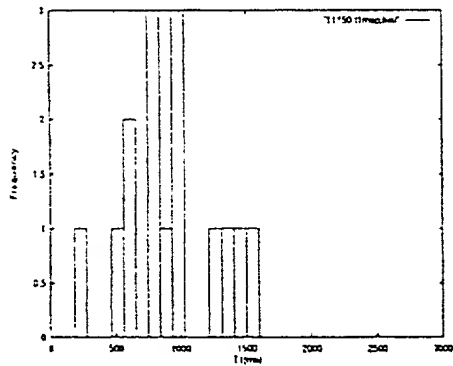
Figure SRL 32

Histology and MRI showing detail of masks 2, 4, 3 and 7 for C78 and C79

C78 qMRI values for mask 2, repair tissue in cartilage compartment

Parameter	Value	(s.e.)
M0(%)	28.6	3.2
T1(ms)	1095	159
T2(ms)	23.0	0.8

Parameter	Value	(s.e.)
Msat/M0	0.215	0.016
T1sat(ms)	75	10
ADC(cm ² /s)	1.4e-05	8.1e-06



ongg 0004-0009-2

x axis - number of pixels with the same value

y axis - range of values.

LHS- top T1, middle Msat/M0, bottom M0.

RHS top T2, mid T1sat, bottom ADC

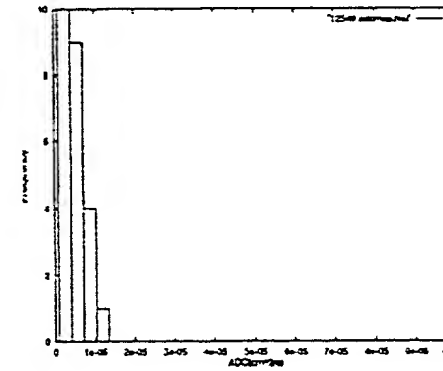
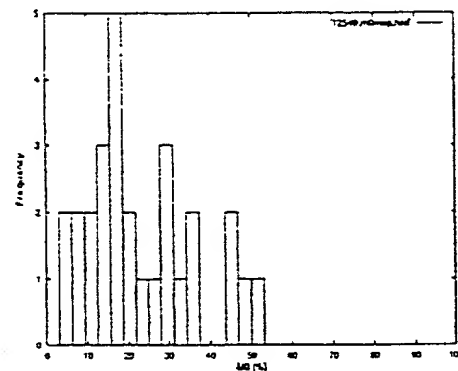
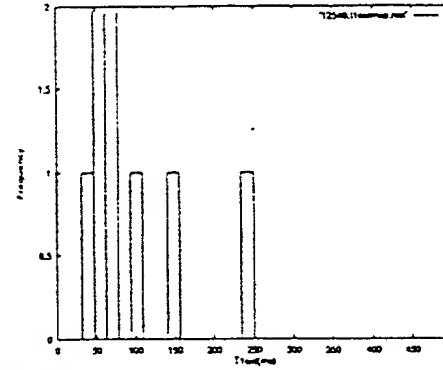
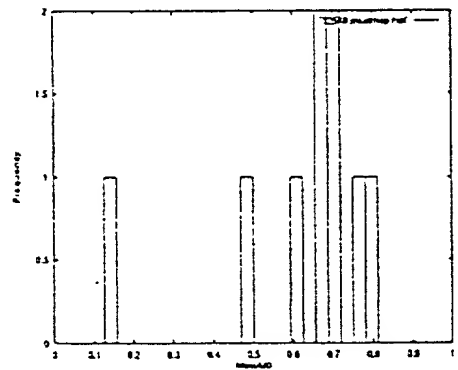
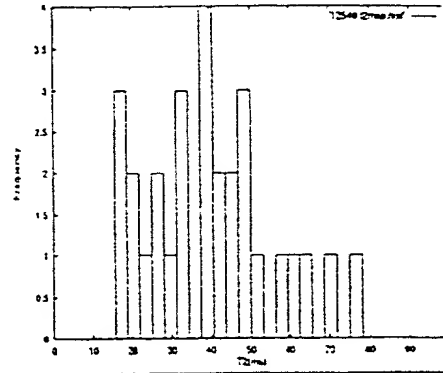
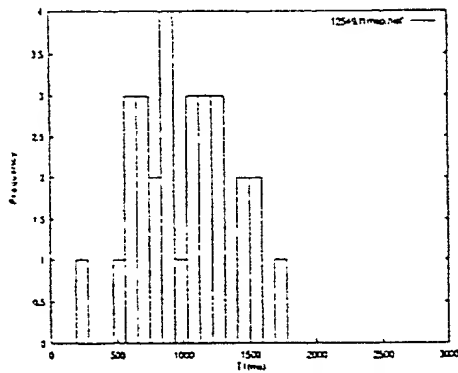
Figure SRL 33 Automated output of histograms for C78 mask 2

Y05040" 0/082360

C78 qMRI values for mask 4, repair tissue in bone compartment

Parameter	Value	(s.e.)
M0(%)	24.0	2.6
T1(ms)	1034	68
T2(ms)	41.0	3.1

Parameter	Value	(s.e.)
Msat/M0	0.641	0.069
T1sat(ms)	101	24
ADC(cm ² /s)	5.1e-06	5.8e-07



ongg 0004-0009-4

x axis - number of pixels with the same value
LHS- top T1,middleMsat/M0,bottom M0.

y axis - range of values.

RHS top T2,mid T1sat,bottom ADC

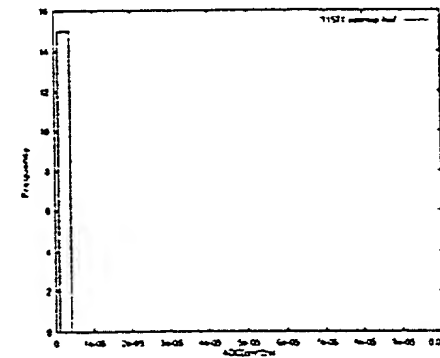
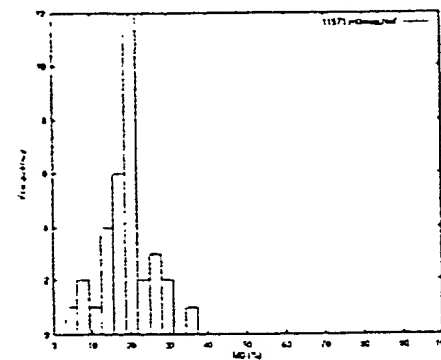
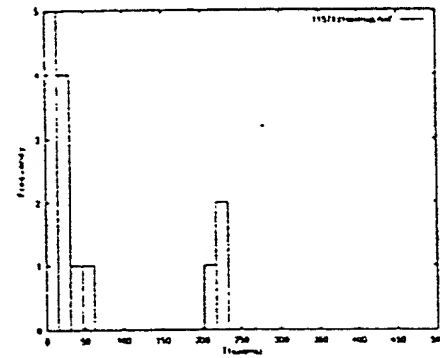
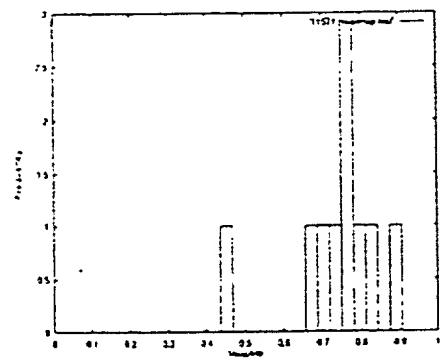
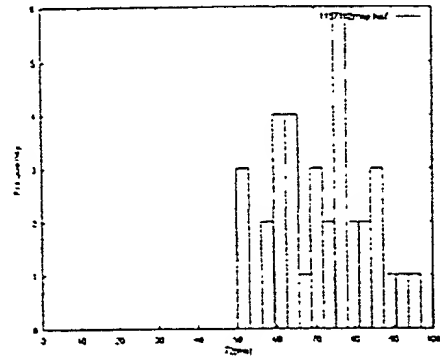
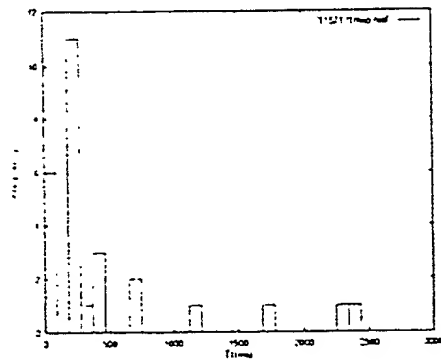
Figure SRL 34 Automated output of histograms for C78 mask 4

T05040 06082860

C79 qMRI values for mask 3, repair tissue in cartilage compartment

Parameter	Value	(s.e.)
M0(%)	20.1	1.2
T1(ms)	427	106
T2(ms)	75.8	2.6

Parameter	Value	(s.e.)
Msat/M0	0.763	0.038
T1sat(ms)	65	24
ADC(cm ² /s)	1.5e-06	1.9e-07



ongg 0004-0009-3

x axis – number of pixels with the same value
LHS- top T1,middleMsat/M0,bottom M0.

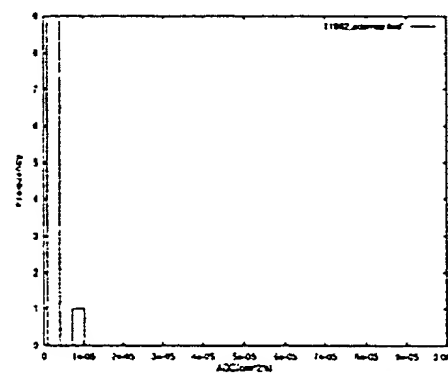
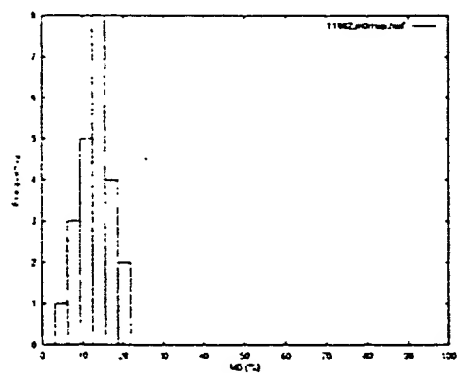
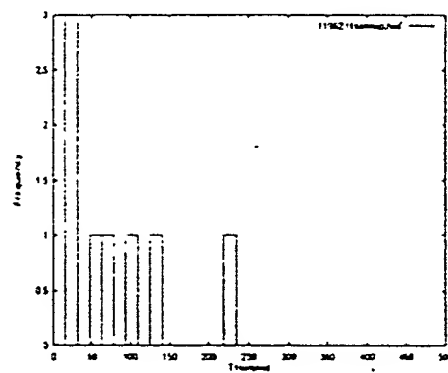
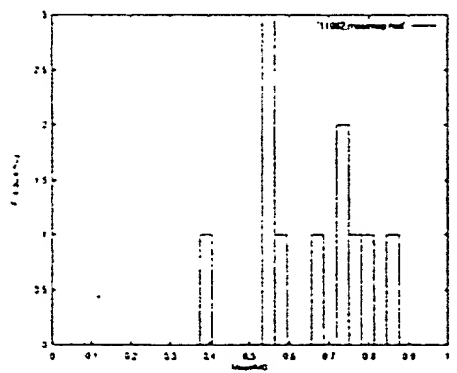
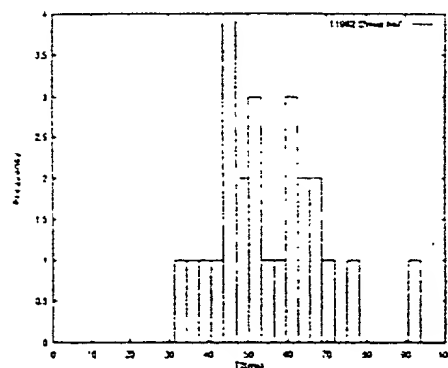
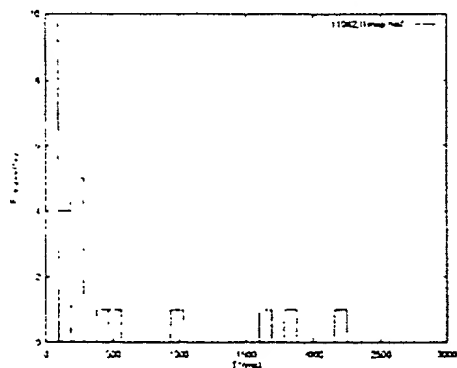
y axis - range of values.

RHS top T2,mid T1sat,bottom ADC

Figure SRL 35 Automated output of histograms for C79 mask 3

C79 qMRI values for mask 7, repair tissue in bone compartment

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	13.5	0.8	Msat/M0	0.674	0.042
T1(ms)	385	125	T1sat(ms)	62	20
T2(ms)	57.0	2.8	ADC(cm ² /s)	2.1e-06	6.5e-07



ongg 0004-0009-7

x axis – number of pixels with the same value
LHS- top T1, middle Msat/M0, bottom M0.

y axis - range of values.

RHS top T2, mid T1sat, bottom ADC

Figure SRL 36 Automated output of histograms for C79 mask 7



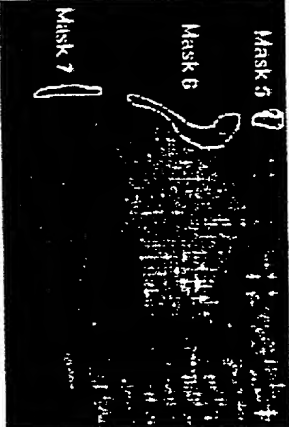

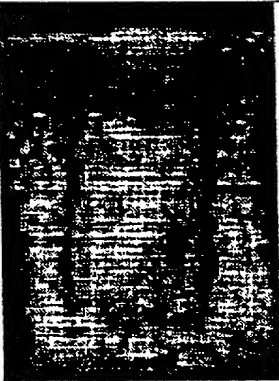
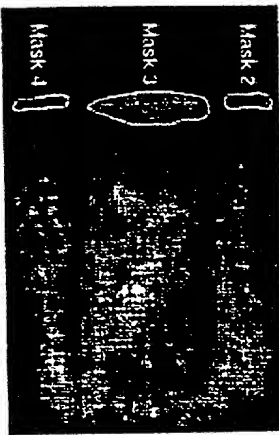

		
C1 Histology	C1 MRI	C1 detail of masks 5, 6 and 7
		
C2 Histology	C2 MRI	C2 detail of masks 2, 3 and 4
	not available	
	C1 mask 6	C2 mask 3

Figure SRL 37

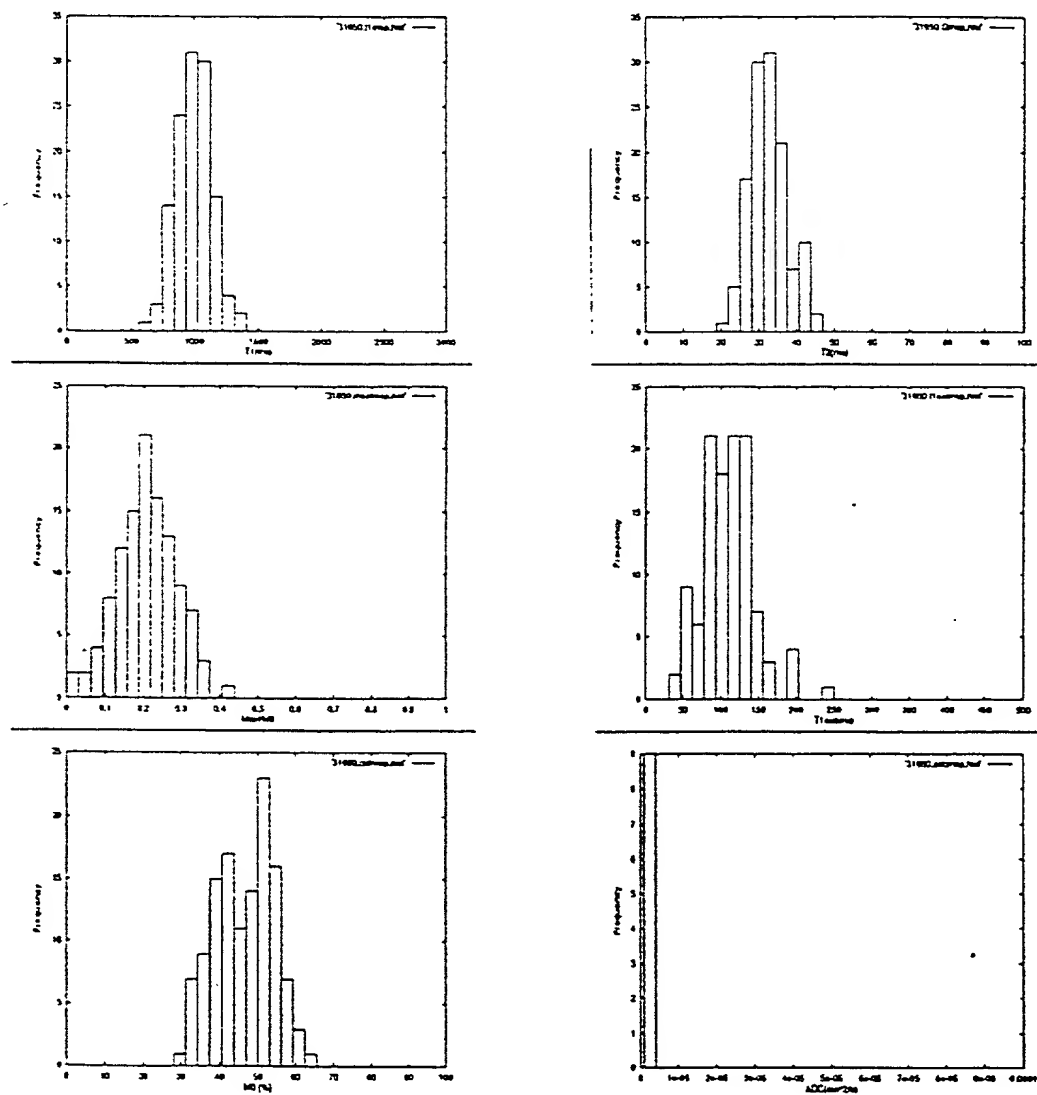
Histology and MRI of spontaneously healed ACD3 defects C1 and C2 at 8 weeks

09828070.040504

C2 mask 3. repair tissue

Parameter	Value	(s.e.)
M0(%)	48.0	0.7
T1(ms)	1028	13
T2(ms)	33.7	0.5

Parameter	Value	(s.e.)
Msat/M0	0.217	0.007
T1sat(ms)	113	3
ADC(cm ² /s)	1.7e-06	3.2e-07



ongg 3804-3809-3

x axis – number of pixels with the same value
 LHS- top T1,middle Msat/M0,bottom M0.

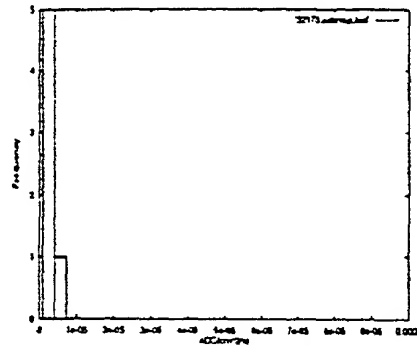
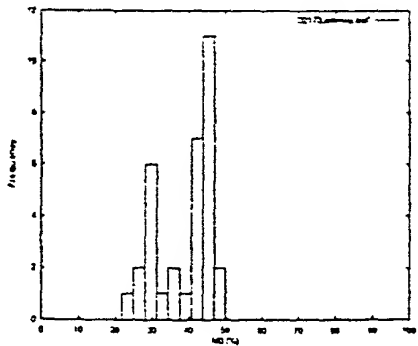
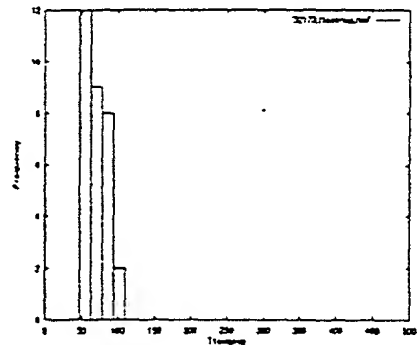
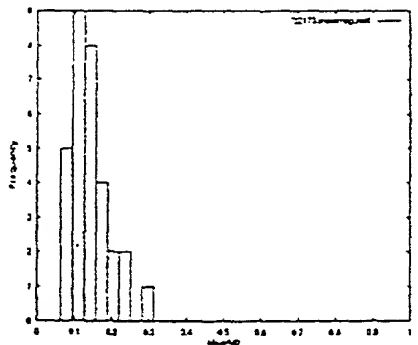
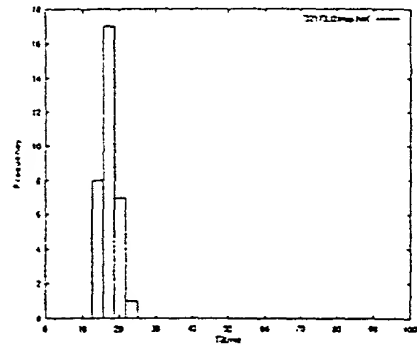
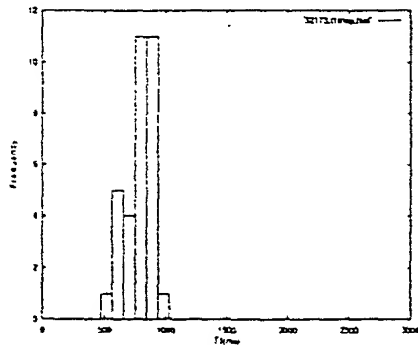
y axis - range of values.
 RHS - top T2,mid T1sat,bottom ADC

Figure SRL 38 Automated output of histograms for C2 mask 3

C2 mask 4, cartilage adjacent to the defect

Parameter	Value	(s.e.)
M0(%)	40.3	1.3
T1(ms)	816	21
T2(ms)	17.9	0.4

Parameter	Value	(s.e.)
Msat/M0	0.144	0.009
T1sat(ms)	71	3
ADC(cm ² /s)	1.9e-06	5.9e-07



ongg 3804-3809

x axis - number of pixels with the same value
LHS- top T1,middleMsat/M0,bottom M0.

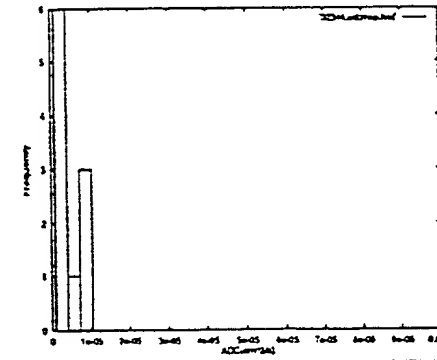
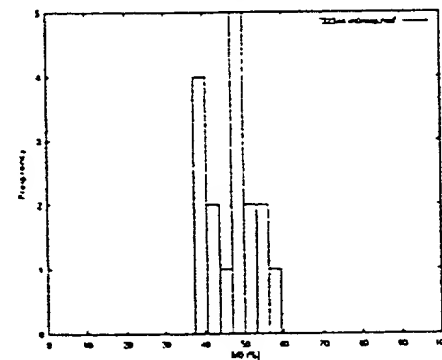
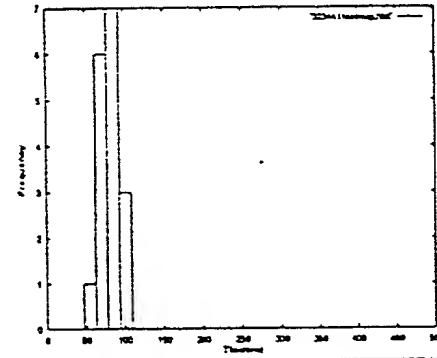
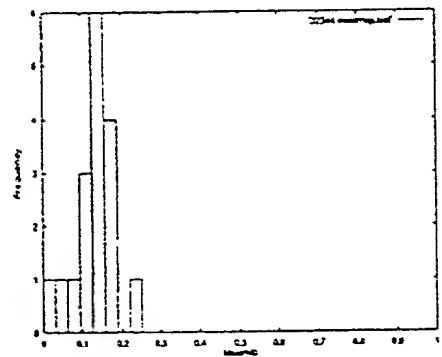
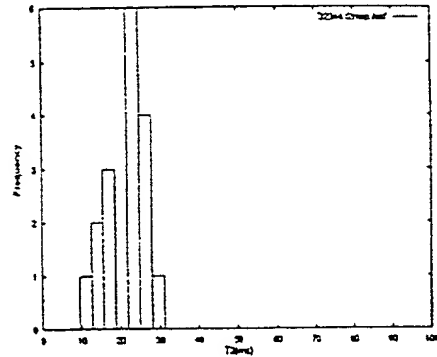
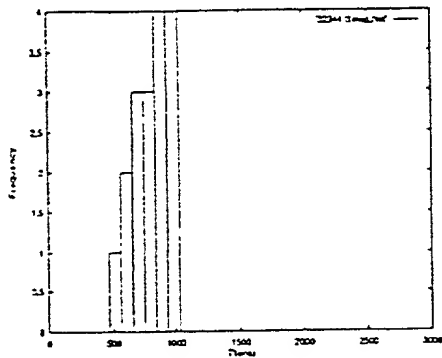
y axis - range of values.

RHS - top T2,mid T1sat,bottom ADC

Figure SRL 39 Automated output of histograms for C2 mask 4

C1 mask 5, cartilage adjacent to the defect

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	48.6	1.5	Msat/M0	0.136	0.012
T1(ms)	830	37	T1sat(ms)	84	4
T2(ms)	22.5	1.4	ADC(cm ² /s)	3.7e-06	7.7e-07



ongg 3804-3809-5

x axis – number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

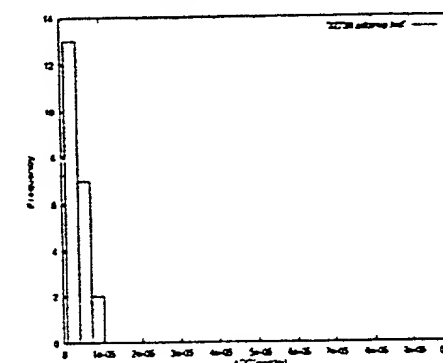
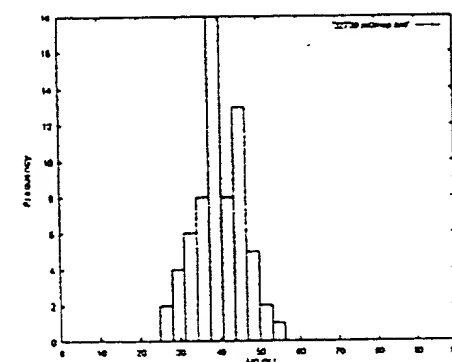
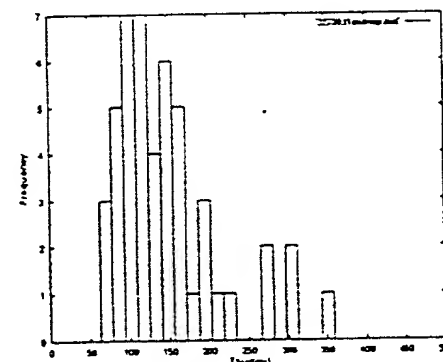
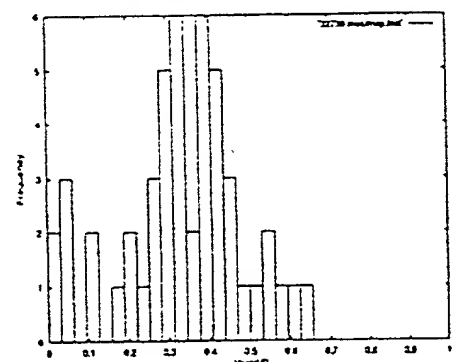
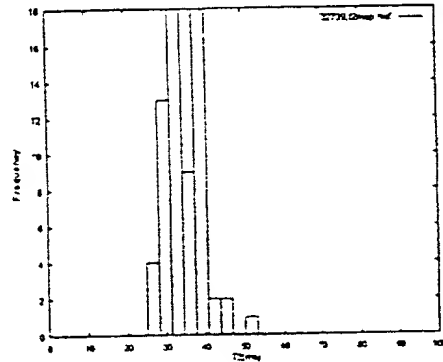
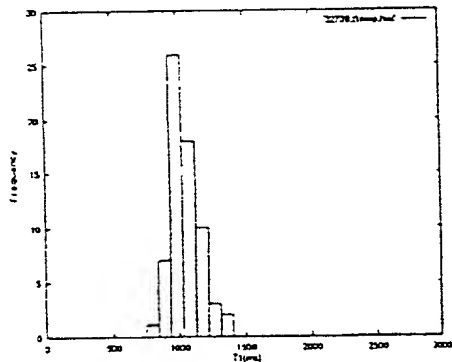
y axis - range of values.
RHS- top T2,mid T1sat,bottom ADC

Figure SRL 40 Automated output of histograms for C2 mask 5

C1 mask 6, repair tissue

Parameter	Value	(s.e.)
M0(%)	41.5	0.8
T1(ms)	1082	15
T2(ms)	36.1	0.6

Parameter	Value	(s.e.)
Msat/M0	0.344	0.023
T1sat(ms)	153	10
ADC(cm2/s)	3.3e-06	4.5e-07



ongg 3804-3809

x axis – number of pixels with the same value
 LHS- top T1, middle Msat/M0, bottom M0.

y axis - range of values.

RHS- top T2, mid T1sat, bottom ADC

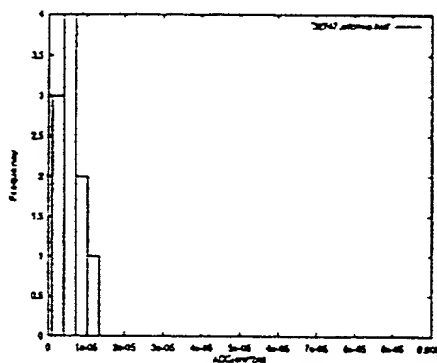
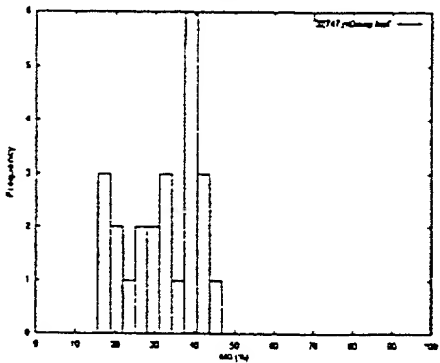
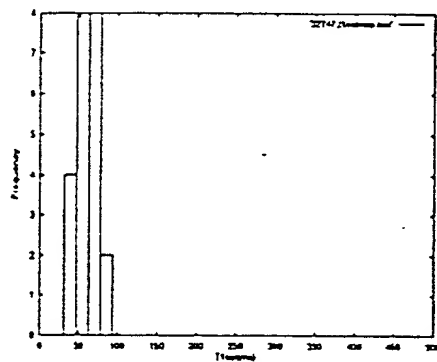
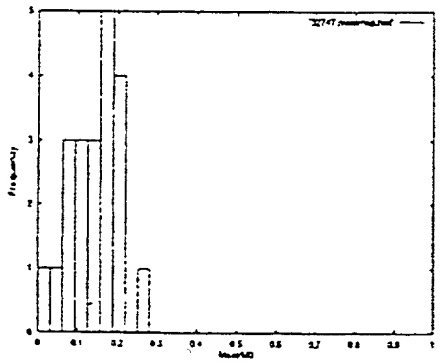
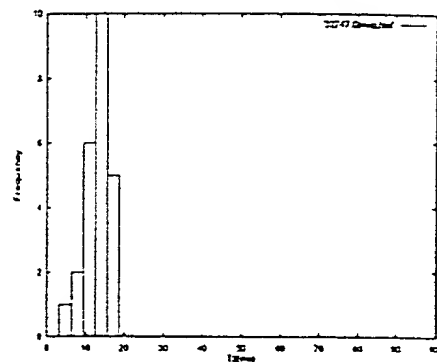
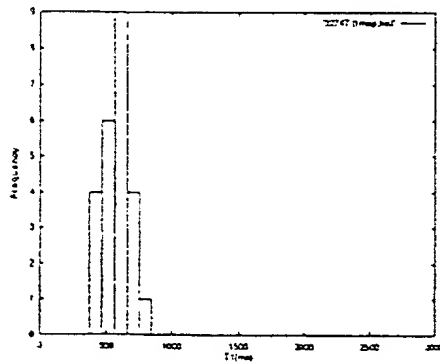
Figure SRL 41 Automated output of histograms for C1 mask 6

T05040"04082360

C1 mask 7, cartilage adjacent to the defect

Parameter	Value	(s.e.)
M0(%)	33.1	1.9
T1(ms)	591	22
T2(ms)	13.5	0.7

Parameter	Value	(s.e.)
Msat/M0	0.145	0.013
T1sat(ms)	62	3
ADC(cm ² /s)	3.9e-06	9.6e-07



ongg 3804-3809-7

x axis - number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

y axis - range of values.
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 42 Automated output of histograms for C1 mask 7

C77 (ACD3 + HAED, no synovium) 8 weeks


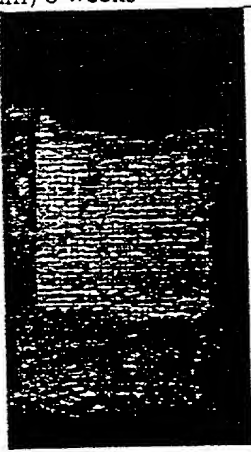
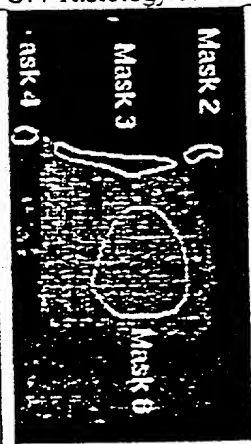


	
C77 Histology of defect	C77 MRI of defect
	
qMRI masks 2,3,4,8	Histology of mask 8, Retained matrix
	
Histology of mask 3, repair tissue	

Figure SRL 43

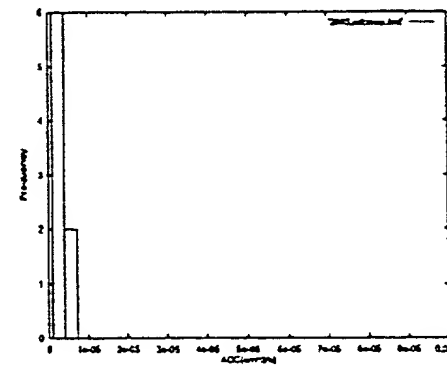
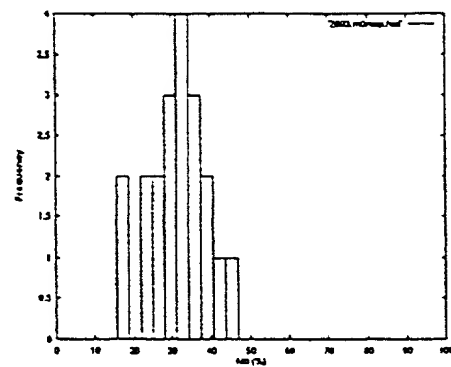
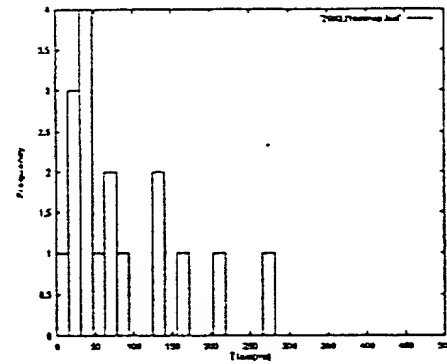
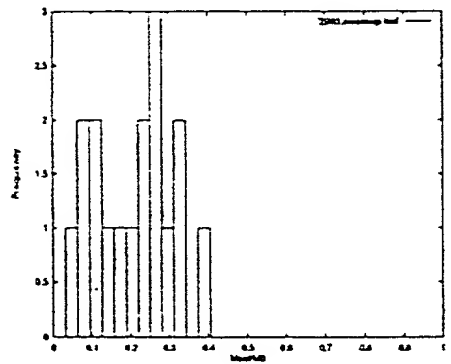
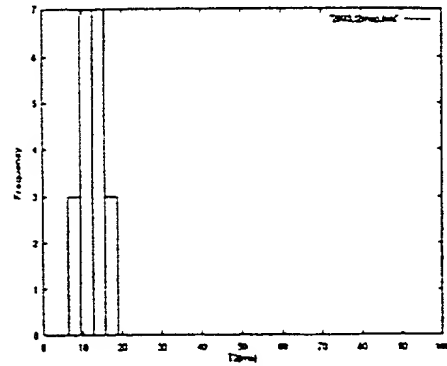
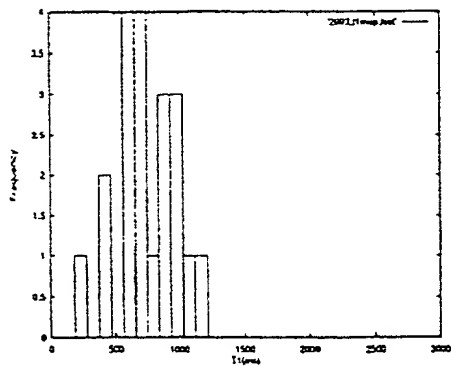
Histology and MRI for C77 (ACD3 + HAED) at 8 weeks

09828070.040501

C77 mask 2

Parameter	Value	(s.e.)
M0(%)	32.4	1.7
T1(ms)	783	55
T2(ms)	13.2	0.8

Parameter	Value	(s.e.)
Msat/M0	0.216	0.027
T1sat(ms)	88	19
ADC(cm2/s)	3.3e-06	5.6e-07



pic 4413-4418-2

x axis - number of pixels with the same value
LHS- top T1,middle Msat/M0,bottom M0.

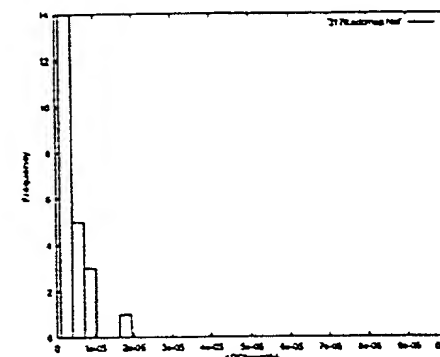
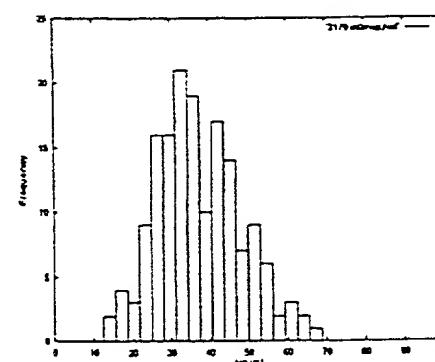
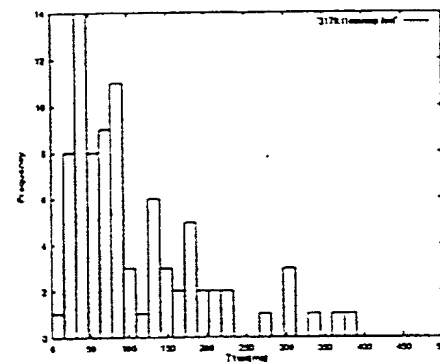
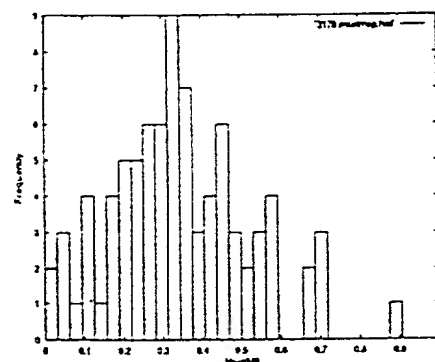
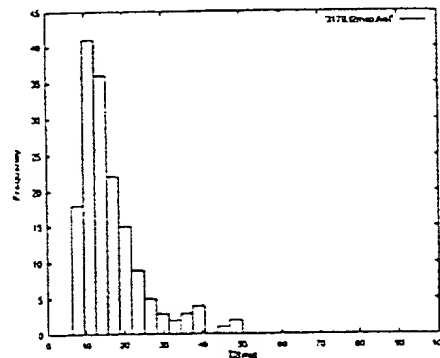
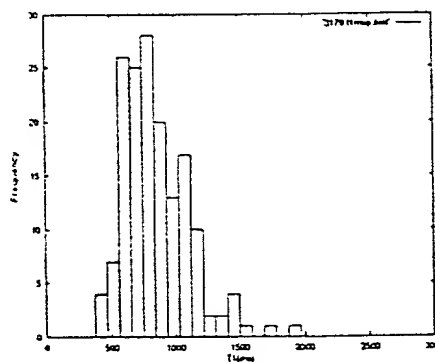
y axis - range of values.
RHS- top T2,mid T1sat,bottom ADC

Figure SRL 44 Automated output of histograms for C77 mask 2

C77 mask 3

Parameter	Value	(s.e.)
M0(%)	38.5	0.9
T1(ms)	884	20
T2(ms)	17.3	0.7

Parameter	Value	(s.e.)
Msat/M0	0.355	0.020
T1sat(ms)	112	10
ADC(cm2/s)	2.4e-06	5.1e-07



pic 4413-4418-3

x axis - number of pixels with the same value
LHS- top T1, middle Msat/M0, bottom M0.

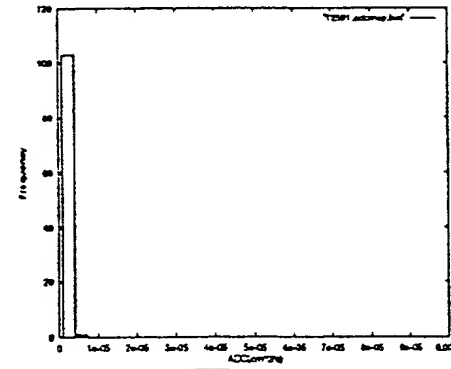
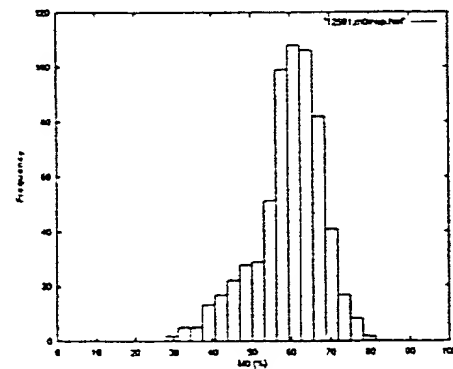
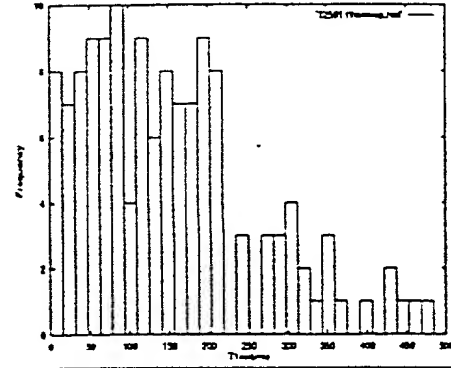
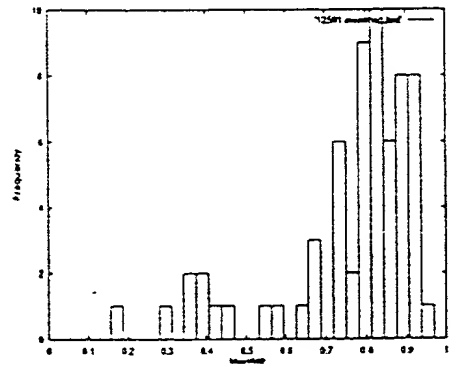
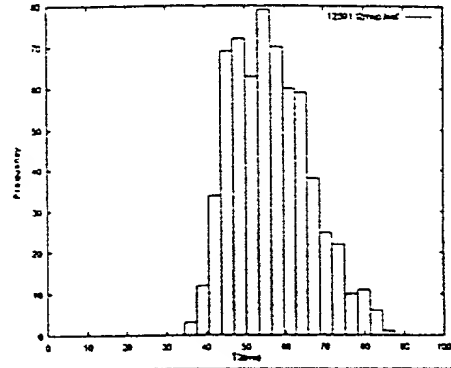
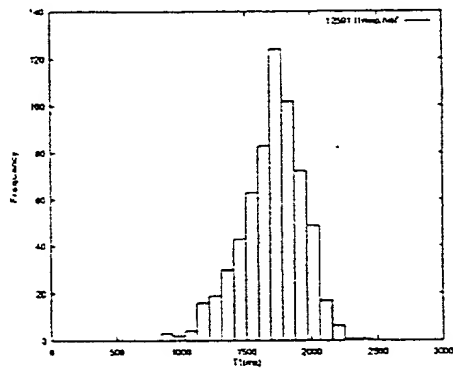
y axis - range of values.
RHS- top T2, mid T1sat, bottom ADC

Figure SRL 45 Automated output of histograms for C77 mask 3

C77 mask 8

Parameter	Value	(s.e.)
M0(%)	61.4	0.4
T1(ms)	1758	10
T2(ms)	58.4	0.4

Parameter	Value	(s.e.)
Msat/M0	0.785	0.023
T1sat(ms)	222	18
ADC(cm2/s)	1.3e-06	6.7e-08



picg 4413-4418-8

x axis - number of pixels with the same value
LHS- top T1,middleMsat/M0,bottom M0.

y axis - range of values.
RHS- top T2,mid T1sat,bottom ADC

Figure SRL 46 Automated output of histograms for C77 mask 8

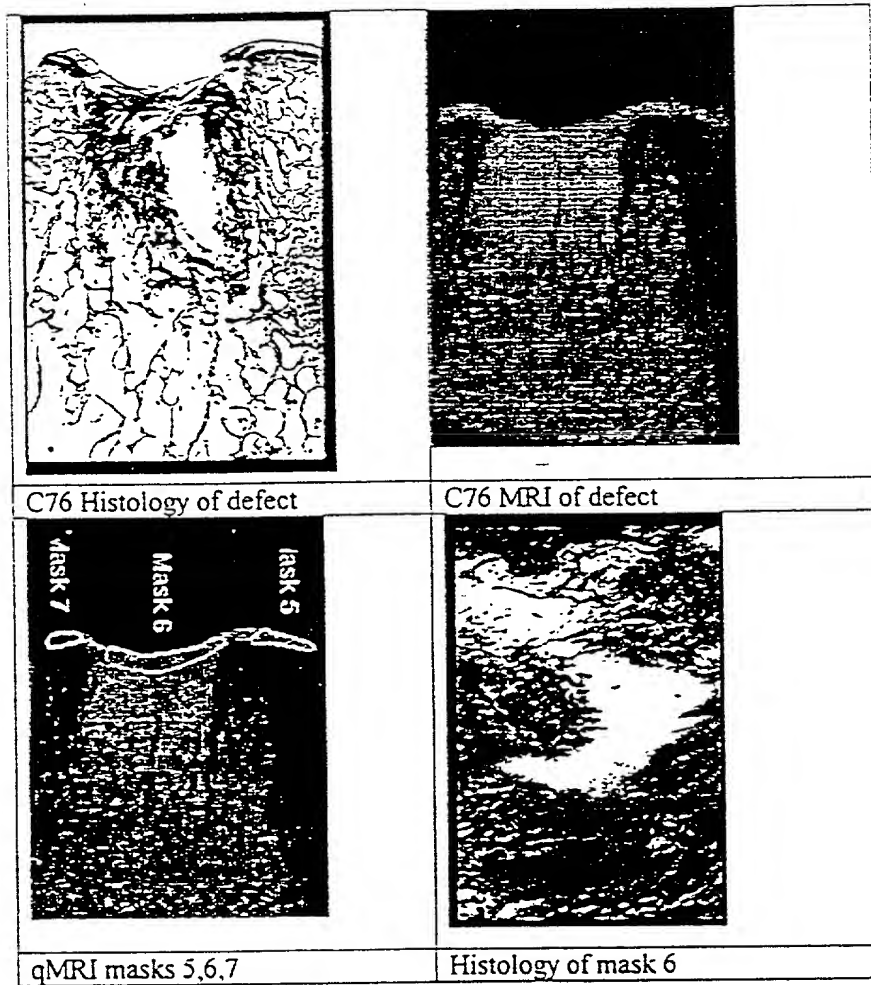


Figure SRL 47

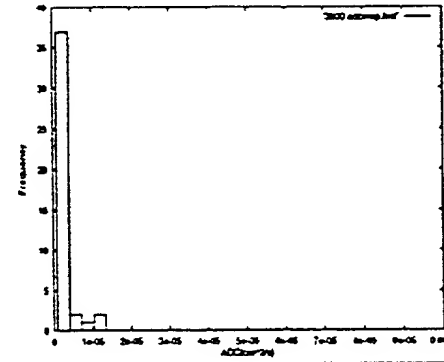
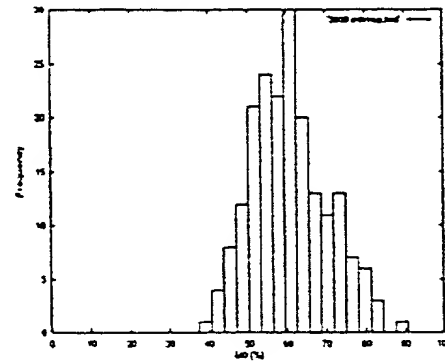
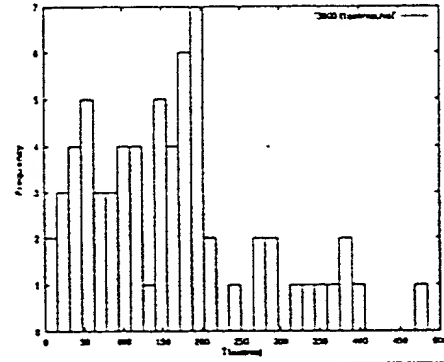
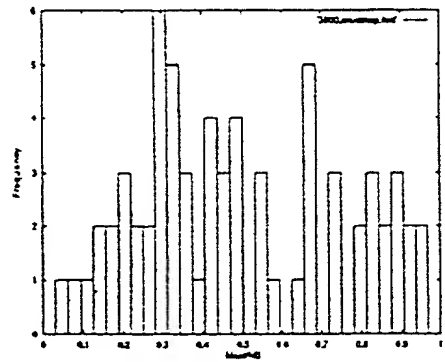
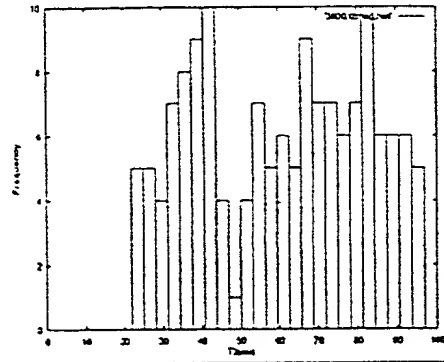
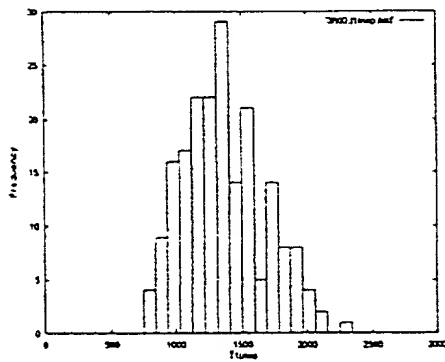
Histology and MRI for C76 (ACD3 + HAED) at 8 weeks

09828070.04501

C76 mask 6, retained matrix + repair tissue

Parameter	Value	(s.e.)
M0(%)	62.6	0.7
T1(ms)	1425	26
T2(ms)	77.0	2.5

Parameter	Value	(s.e.)
Msat/M0	0.509	0.032
T1sat(ms)	197	20
ADC(cm ² /s)	1.8e-06	2.5e-07



picg 4413-4418-6

x axis - number of pixels with the same value
LHS- top T1, middle Msat/M0, bottom M0.

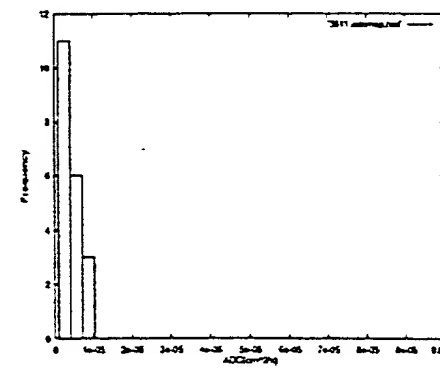
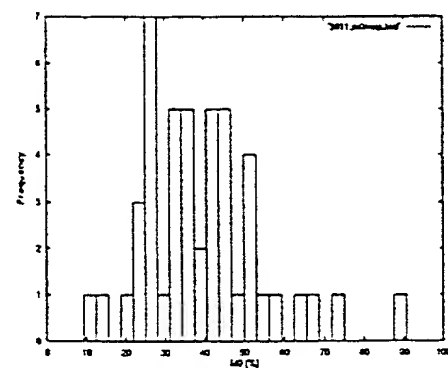
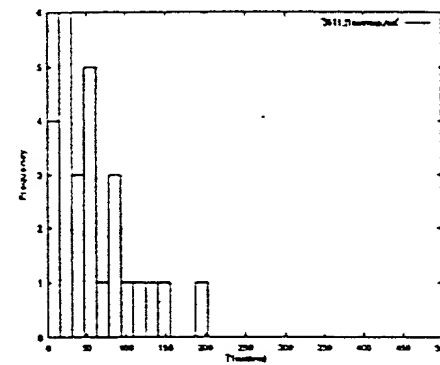
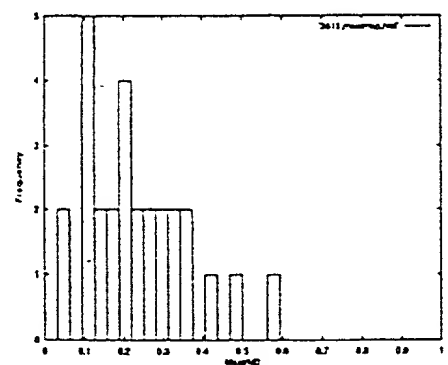
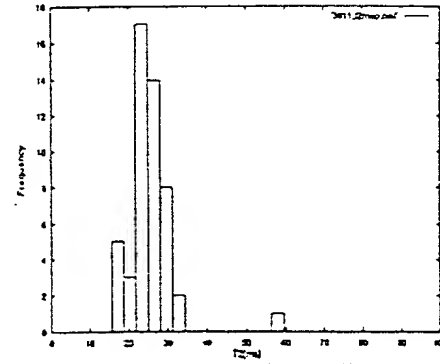
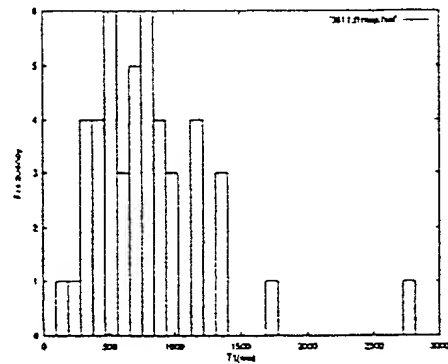
y axis - range of values.

RHS- top T2, mid T1sat, bottom ADC

Figure SRL 48 Automated output of histograms for C76 mask 6

C76 mask 5, cartilage adjacent to the defect

Parameter	Value	(s.e.)	Parameter	Value	(s.e.)
M0(%)	40.7	2.3	Msat/M0	0.241	0.025
T1(ms)	864	83	T1sat(ms)	62	10
T2(ms)	26.3	0.9	ADC(cm ² /s)	3e-06	4.7e-07



picg 4413-4418-5

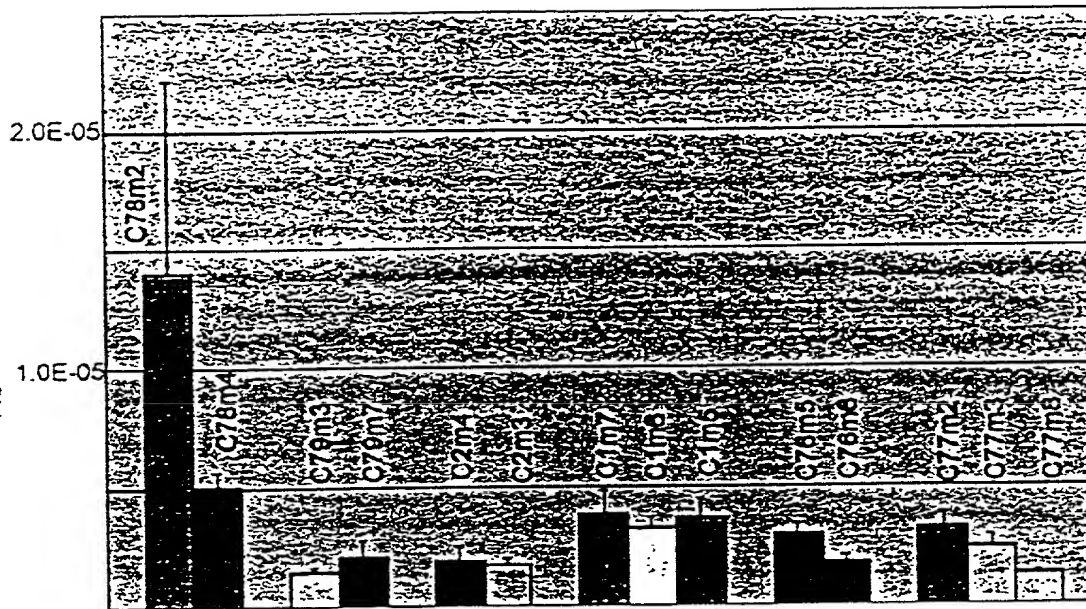
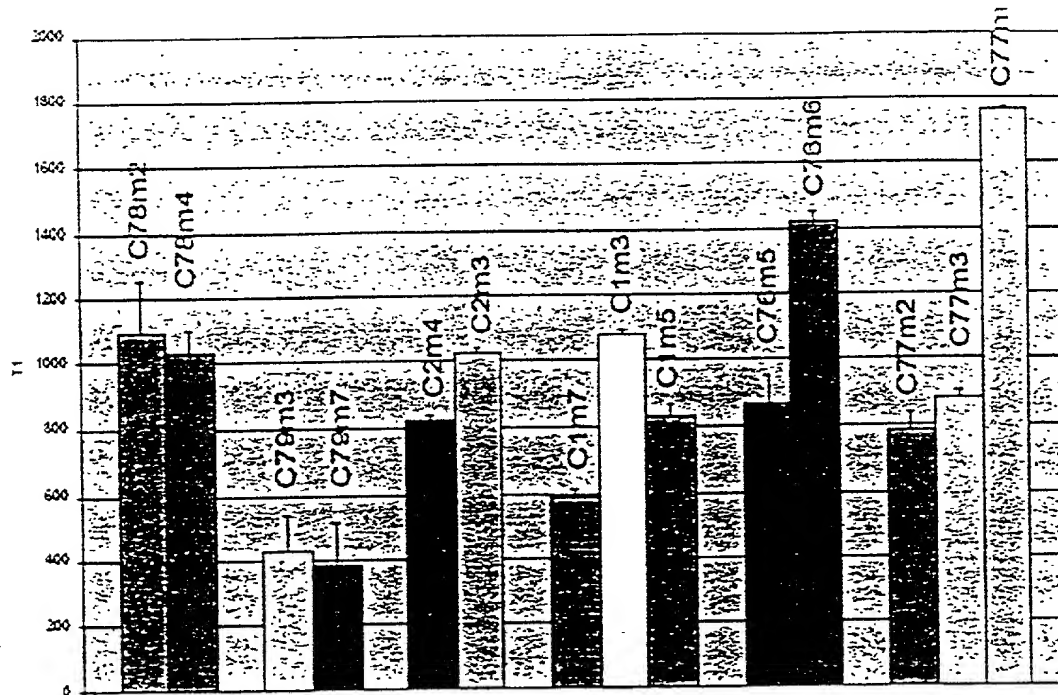
x axis - number of pixels with the same value

y axis - range of values.

LHS- top T1,middle Msat/M0,bottom M0.

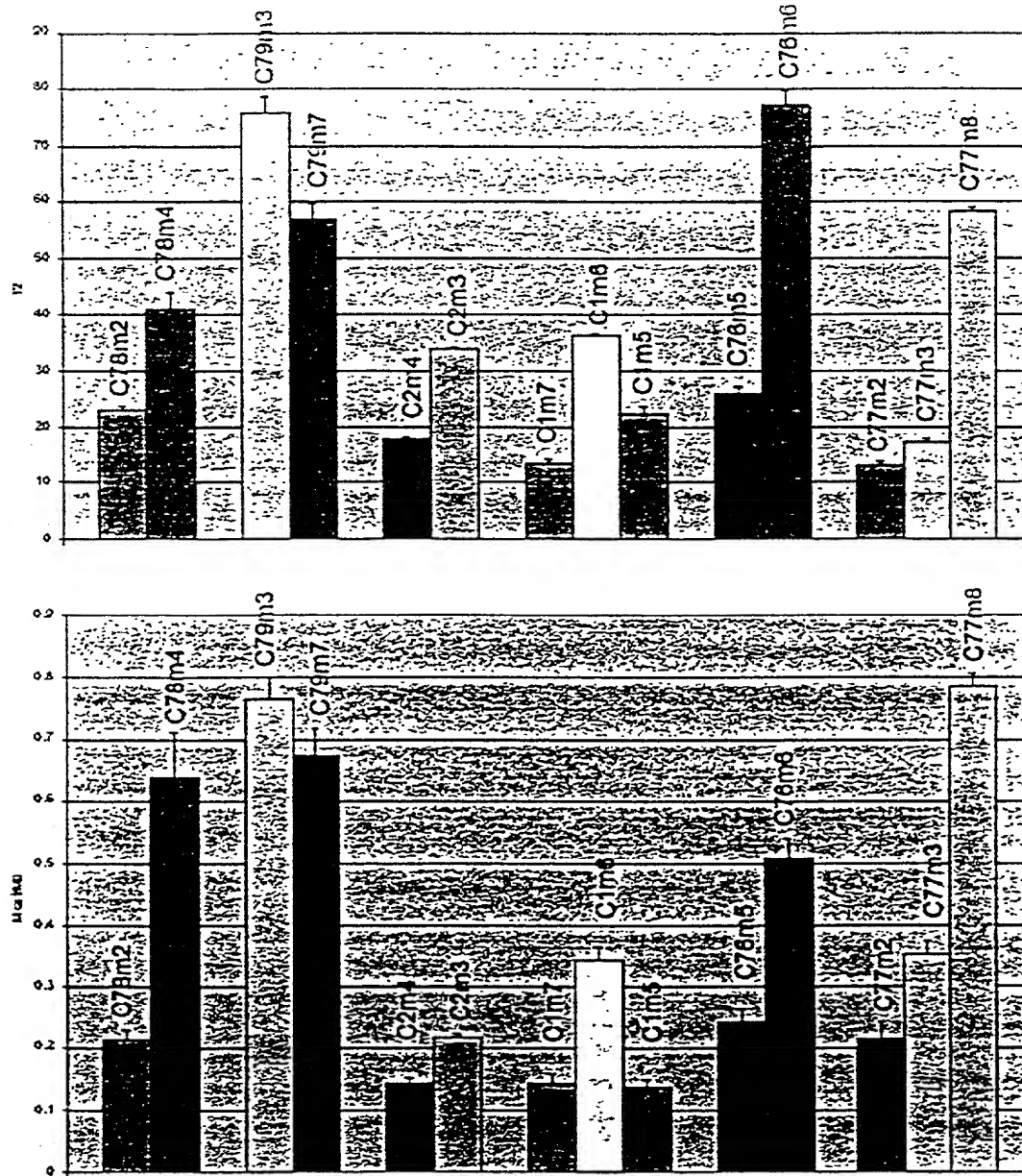
RHS - top T2,mid T1sat,bottom ADC

Figure SRL 49 Automated output of histograms for C76 mask 5



Summary of T1 and ADC in ACD3 defects

Figure SRL 50a. Summary of mean values of T1 (above) and ADC (below) for repair tissue in ACD3 defects C1, C2, C76, C77, C78 and C79.



Summary of T_2 and M_{sat}/M_0 in ACD3 defects

Figure SRL 50b. Summary of mean values of T_2 (above) and M_{sat}/M_0 (below) for repair tissue in ACD3 defects C1, C2, C76, C77, C78 and C79.

3D data set C137 slices 1-16

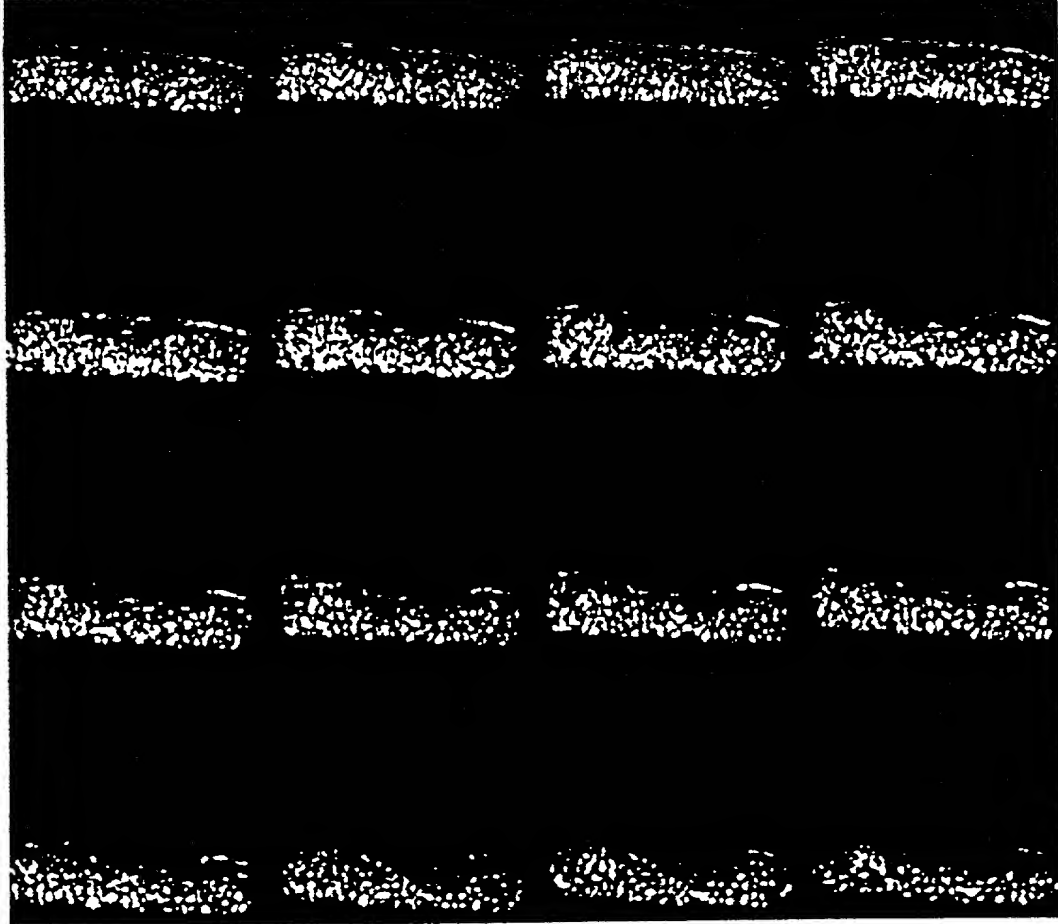


Figure SRL 51a

Adjacent slices (150μm) from a 3D data set showing views from one side of defect C137 (virtual ACD1 + PEG Triacrylate) to the other

3D data set C137 slices 17-32

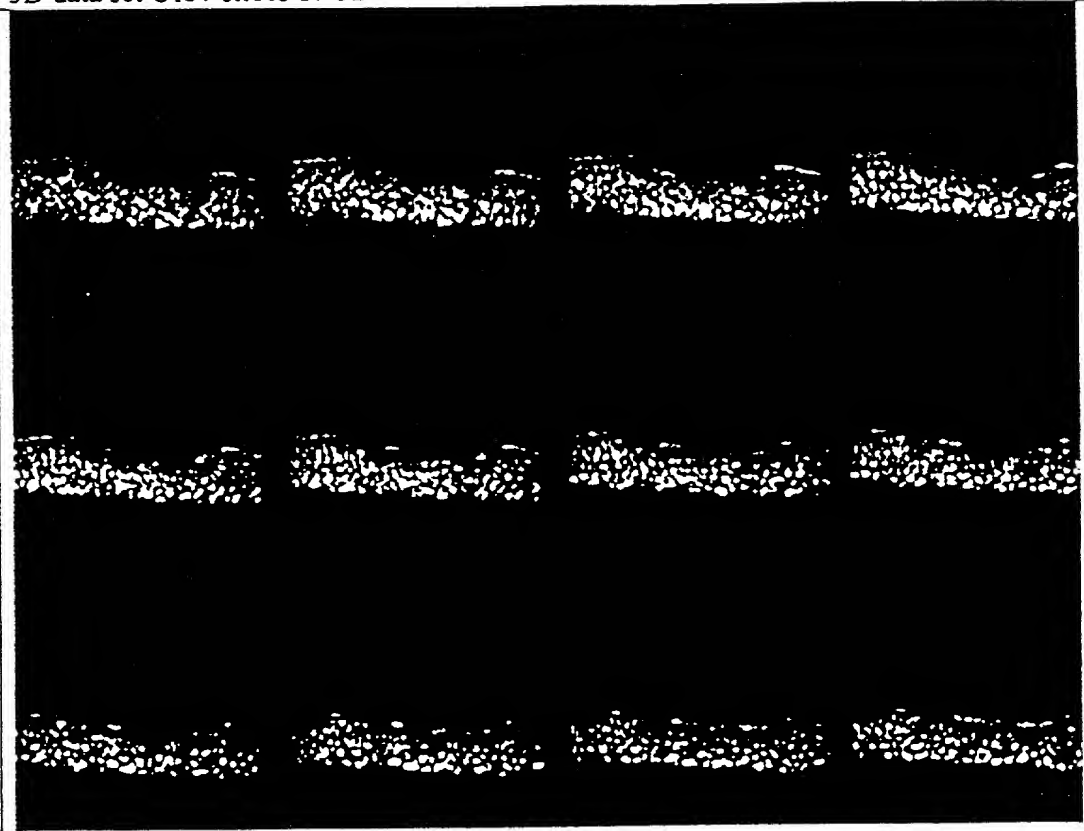


Figure SRL 51b

Adjacent slices (150 μ m) from a 3D data set showing views from one side of defect C137 (virtual ACD1 + PEG Triacrylate) to the other

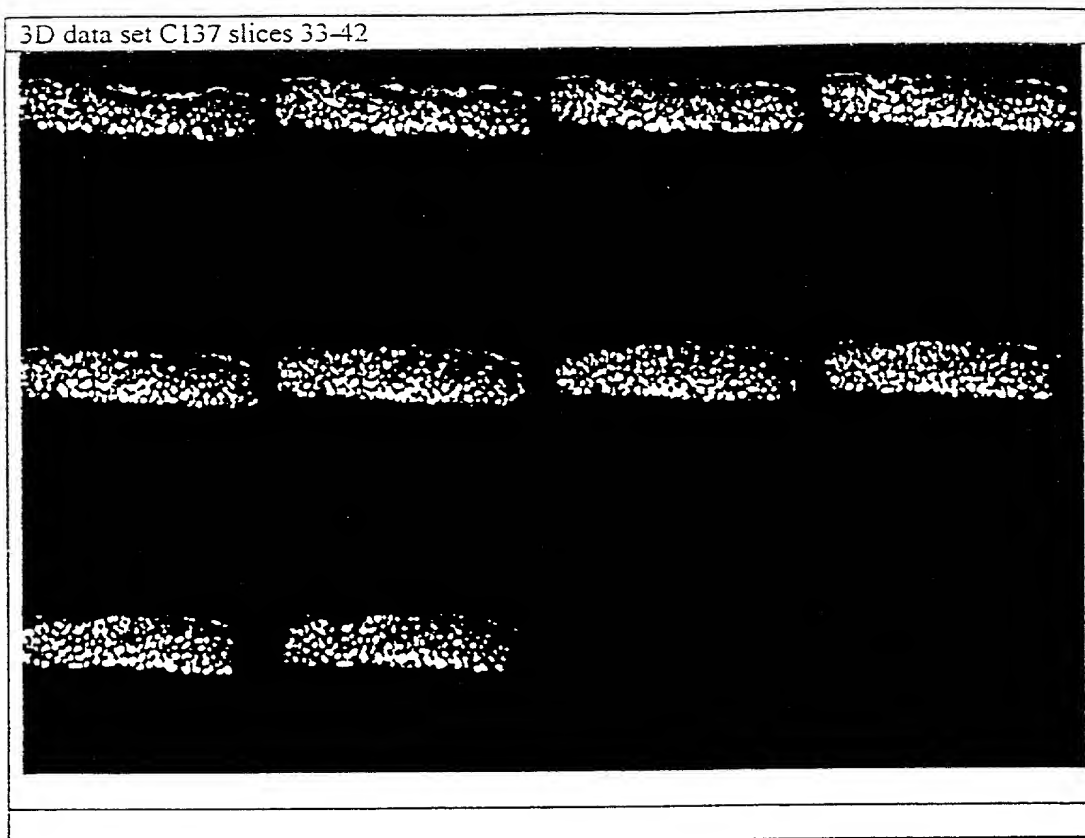


Figure SRL 51c

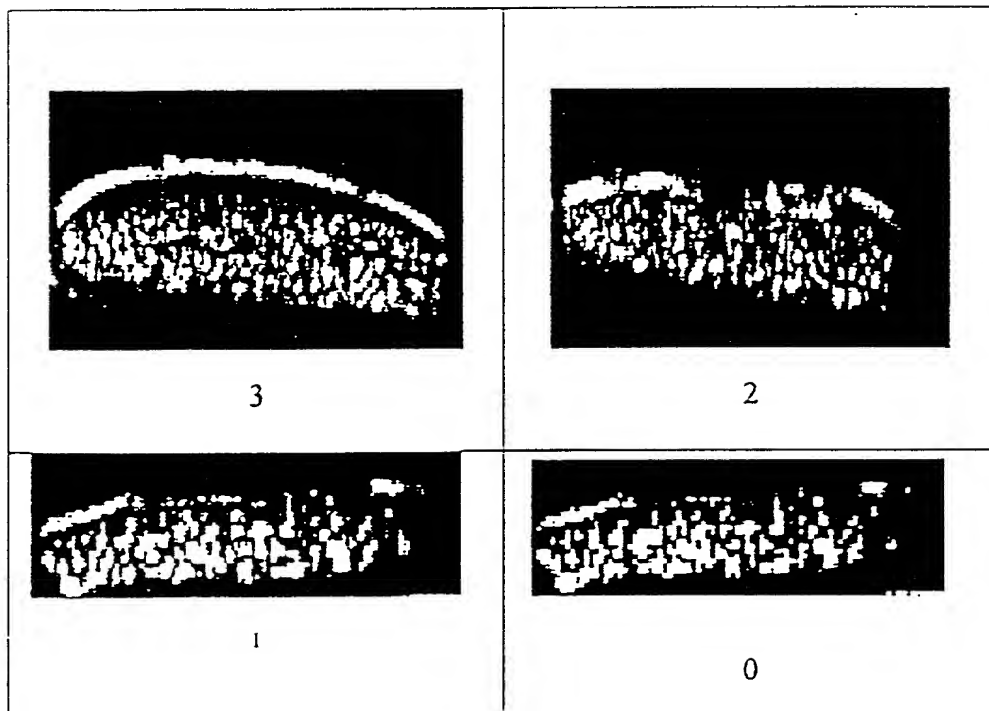
Adjacent slices (150 μ m) from a 3D data set showing views from one side of defect C137 (virtual ACD1 + PEG Triacrylate) to the other

0922070.040504

Scoring ACD1 defects from 3-D MRI scans

Degree of filling of the repair tissue in the defect

- 0 0-20% filling.
- 1 21-40% filling.
- 0 41-70% filling
- 1 70-100% filling.



Sagittal view of defects from a 3D data set

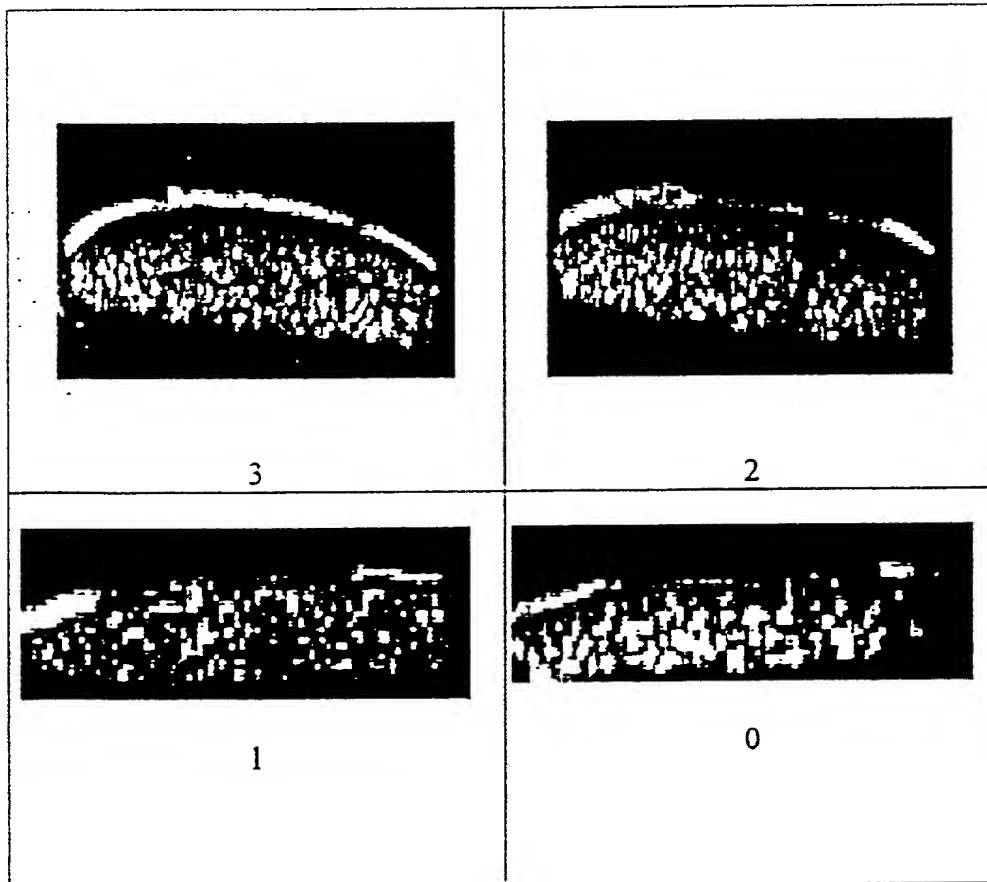
Figure SRL 52

Scoring ACD1 defects from 3-D MRI scans. Degree of filling in the defect

Scoring ACD1 defects from 3-D MRI scans

Integration of the repair tissue to the surrounding cartilage

- 0 No integration to the sides or bone-cartilage interface.
- 1 Minimal integration (20-40%) to the sides or bone-cartilage interface.
- 2 Moderate integration (41-90%) to the sides or bone-cartilage interface.
- 3 Full integration (91-100%) to the sides and bone-cartilage interface.



Sagittal view of defects from a 3D data set

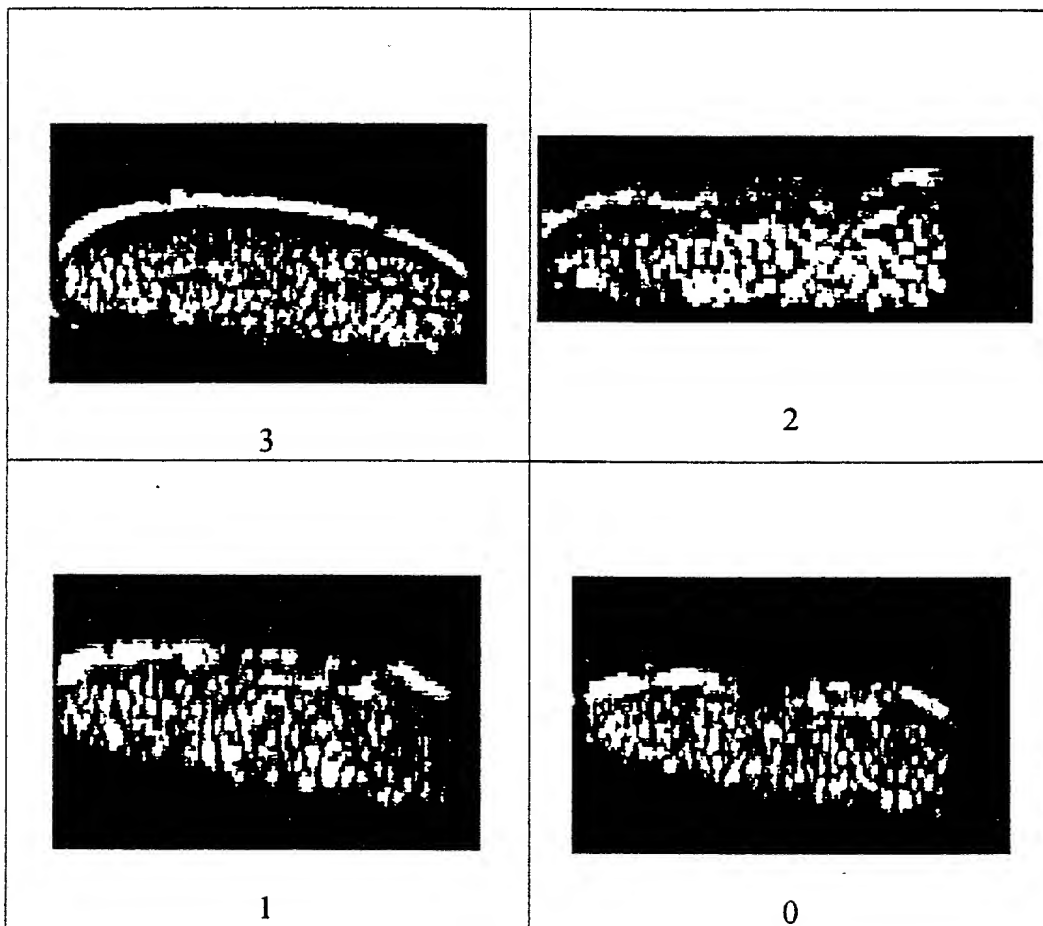
Figure SRL 53

Scoring ACD1 defects from 3-D MRI scans. Integration of repair tissue in the defect

Scoring ACD1 defects from 3-D MRI scans

Surface smoothness of the repair tissue

- 0 Marked fraying extending to the bone surface in the repair tissue.
- 1 Fraying limited to within the substance of the repair tissue.
- 2 No fraying but the surface appears rough and wavy.
- 3 Smooth surface.



Sagittal view of defects from a 3D data set

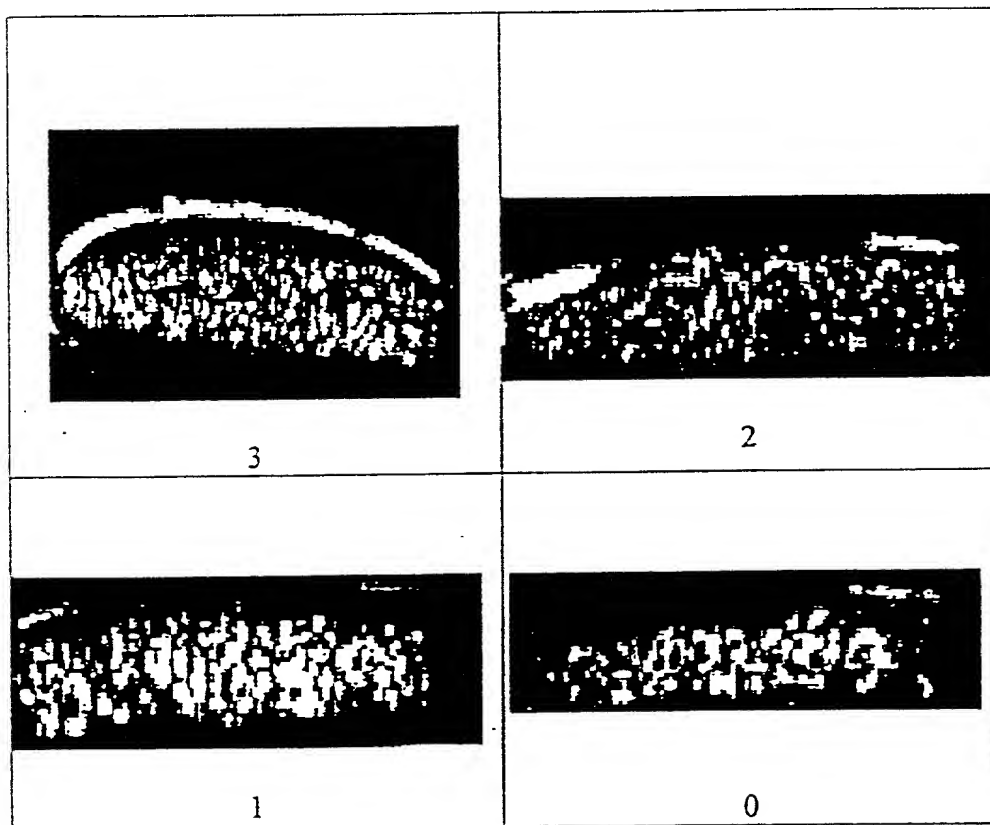
Figure SRL 54

Scoring ACD1 defects from 3-D MRI scans. Smoothness of surface repair

Scoring ACD1 defects from 3-D MRI scans

Disruption of subchondral and trabecular bone

- 0 SC bone plate absent with marked loss of trabecular bone.
- 1 SC bone plate broken with disruption of the trabecular bone pattern.
- 2 SC bone plate interrupted with no alteration to the trabecular bone pattern.
- 3 SC bone plate normal with normal trabecular bone underneath.



Sagittal view of defects from a 3D data set

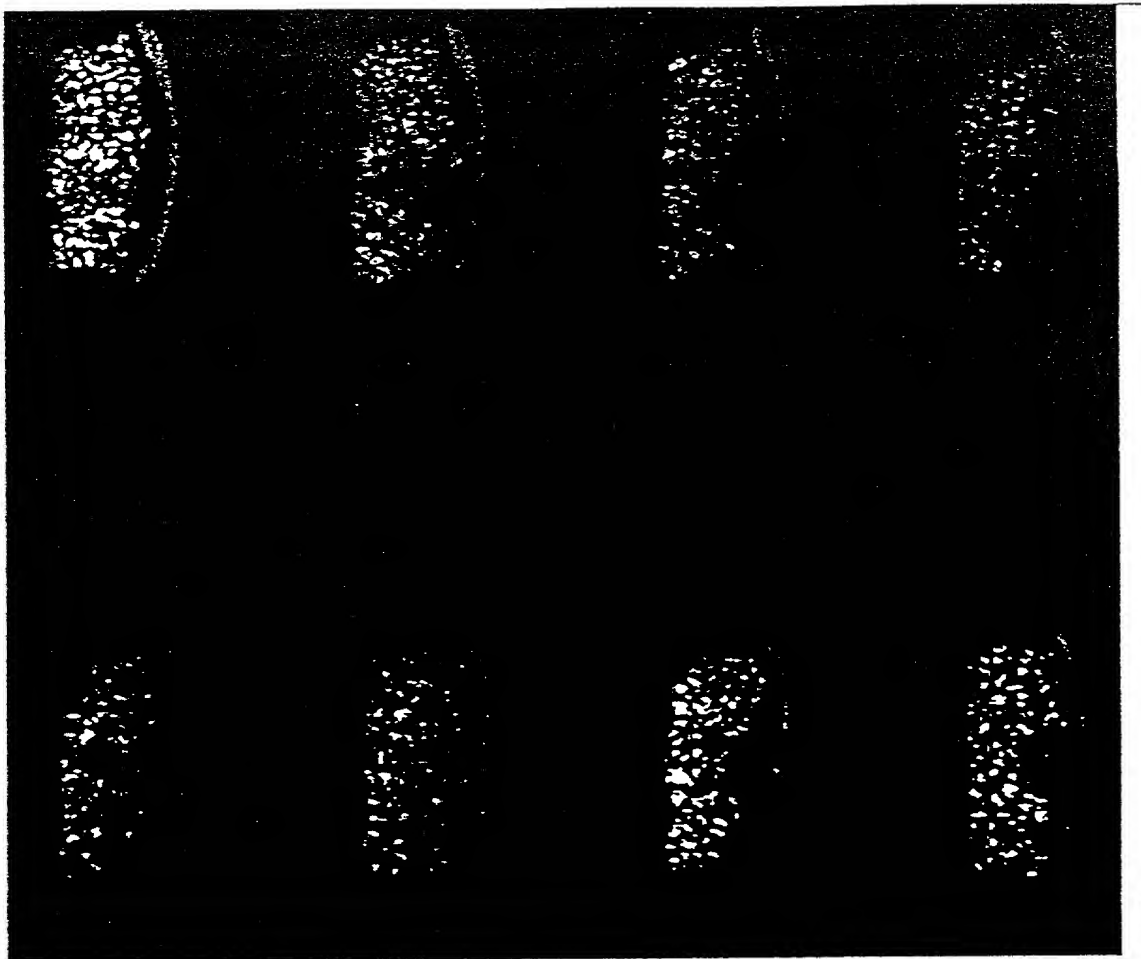
Figure SRL 55. Scoring ACD1 defects from 3-D MRI scans.
Disruption of trabecular and subchondral bone

Scoring ACD1 defects from 3D MRI scans

G	Specimen	Filling	Integration	Surface	Bone	Signal	Total
G84	C151	3	3	2	3	2	13
G45	C118	0	0	0	3	0	3
G80	C123	3	1	2	2	2	10
+G69	C132	0	0	0	1	0	1
G70	C133	0	0	0	1	0	1
G63	C129	3	2	2	3	2	12
G81	C126	0	0	0	2	0	2
G77	C121	0	0	0	3	0	3
G56	C119	0	0	0	3	1	4
G68	C134	0	0	0	1	0	1
G61	C137	0	0	0	2	1	3
G78L	C139	1	1	1	2	2	7
G78R	C138	0	1	0	2	1	4
G73	C143	2	1	1	3	1	8
G66	C145	0	0	0	2	1	3
G83	C146	0	0	0	3	0	3
K2	C149	1	0	0	3	1	5
G86	C156	1	1	0	3	1	6
G87	C157	2	1	1	2	2	8
G52	C116	0	0	0	3	1	4
G58	C131	2	1	1	3	2	9
G59	C128	3	2	1	3	2	11

Figure SRL 56. Table summarising scores of ACD1 defects from 3-D MRI scans.

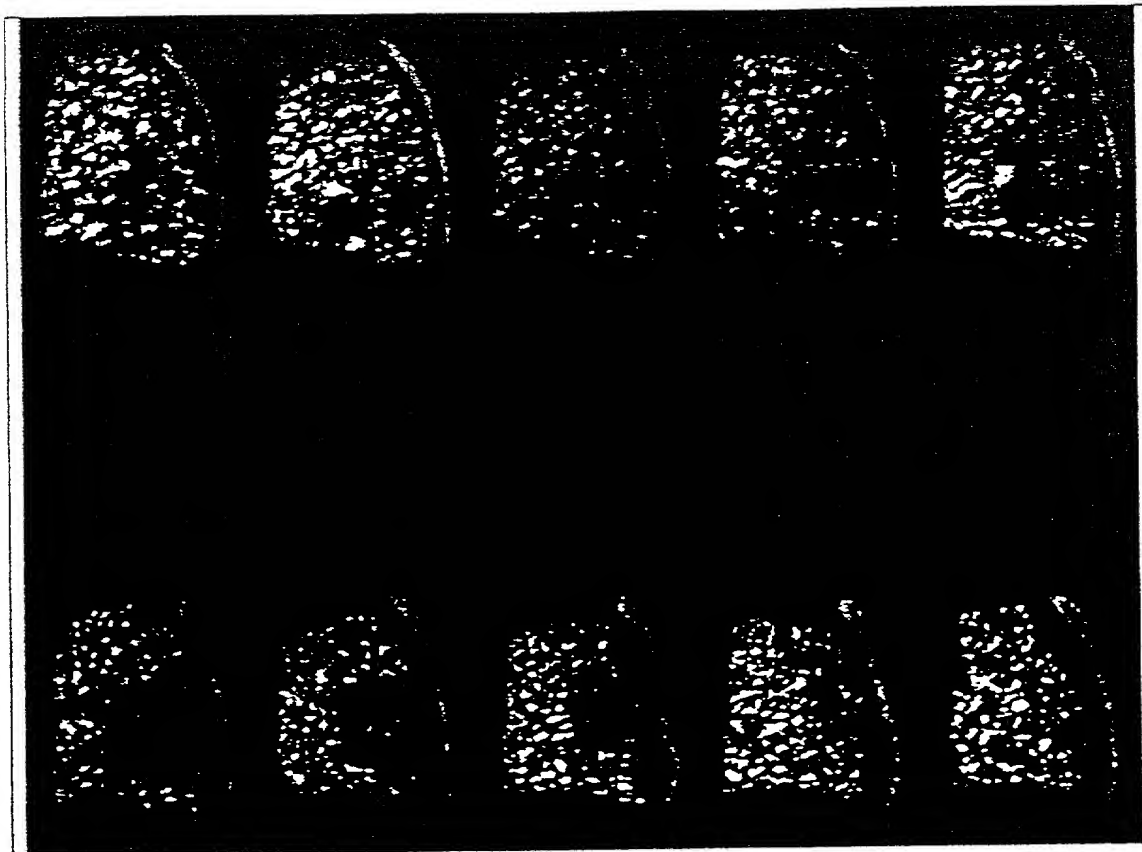
FD-5040 04032260



G34 Right medial condyle (C181)

Score : filling -2 , integration-1, surface-2, bone-1, signal-3. Total 9 [max 15]

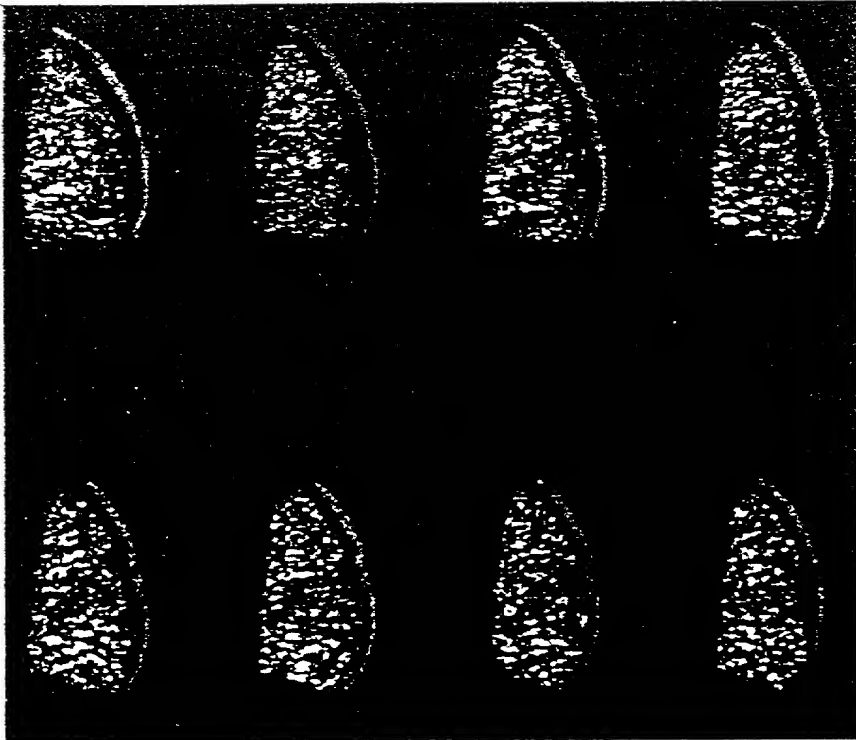
Figure SRL 57 Slices from a 3D data set of C181 showing views and scoring of an OCT graft in the medial condyle



G34 Right lateral condyle (C182)

Score : filling -2 , integration-1, surface-2, bone-1, signal-3. Total 9 [max 15]

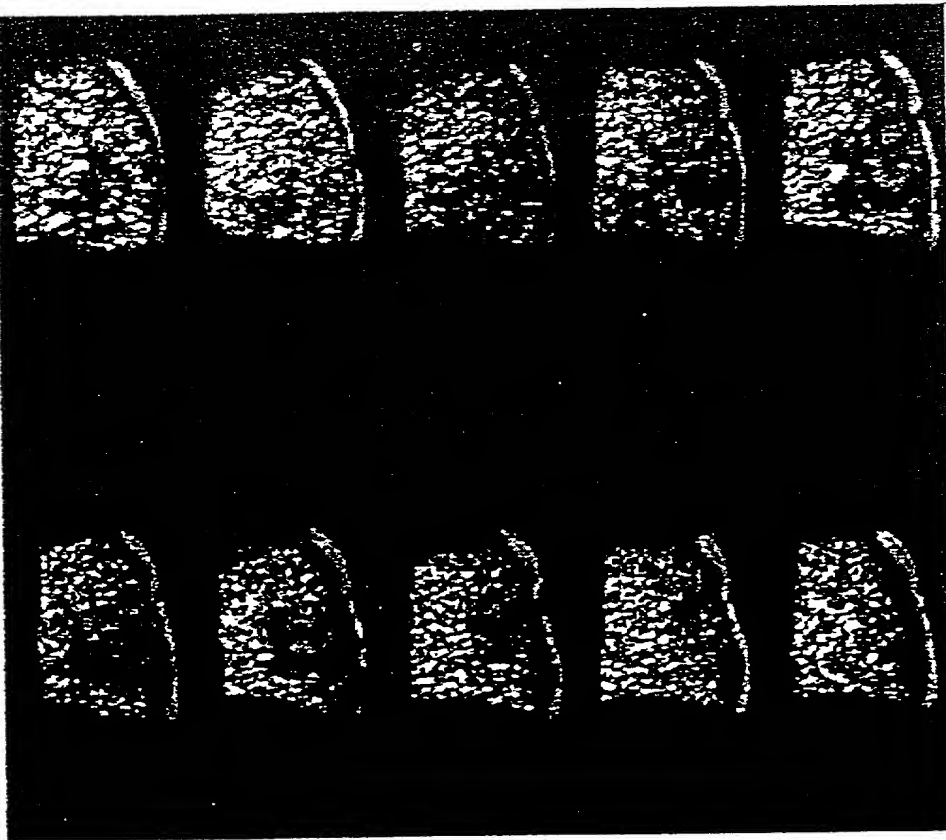
Figure SRL 58 Slices from a 3D data set of C182 showing views and scoring of an OCT graft in the lateral condyle



G33 Right lateral condyle (C174)

Score : filling -3 , integration-3, surface-1, bone-3, signal-3. Total 13 [max 15]

Figure SRL 59 Slices from a 3D data set of C174 showing views and scoring of an OCT graft in the lateral condyle



G33 Right medial condyle (C173)

Score : filling -3 , integration-2, surface-2, bone-1, signal-3. Total 11 [max 15]

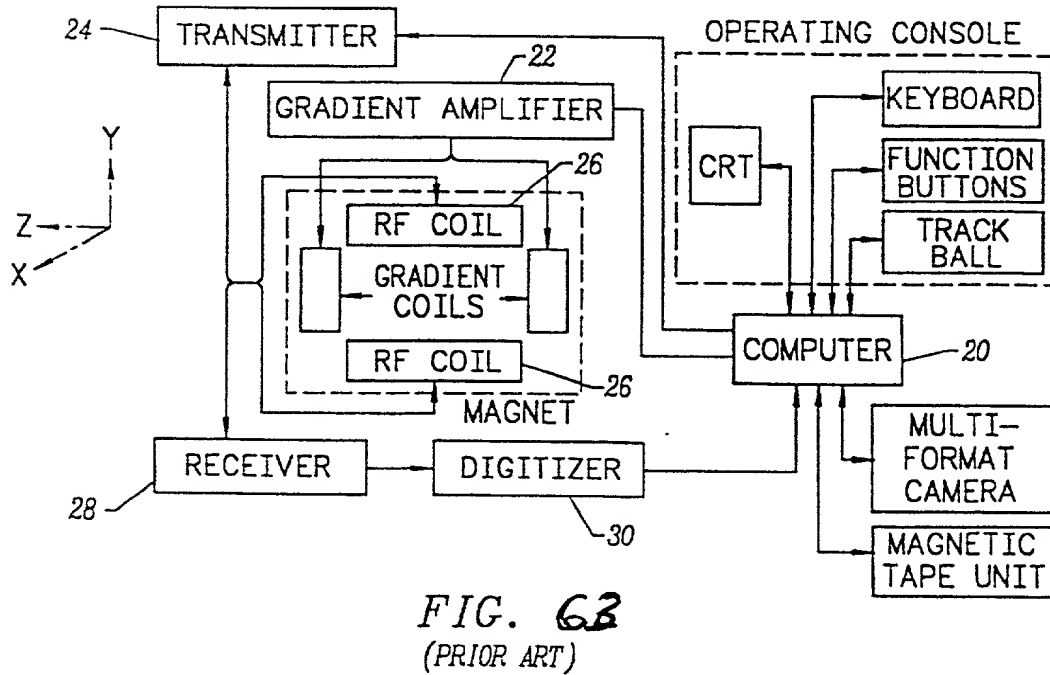
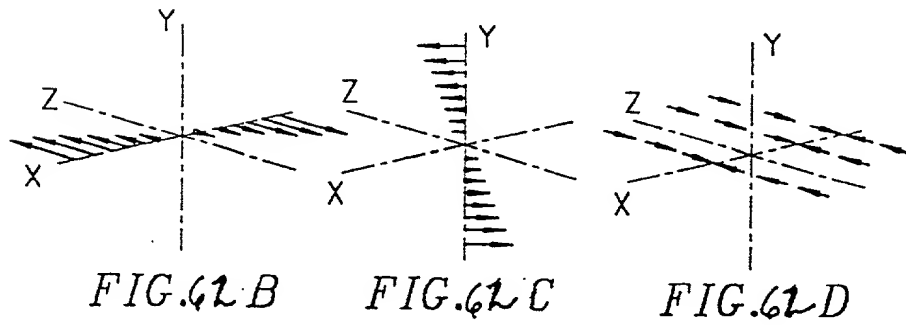
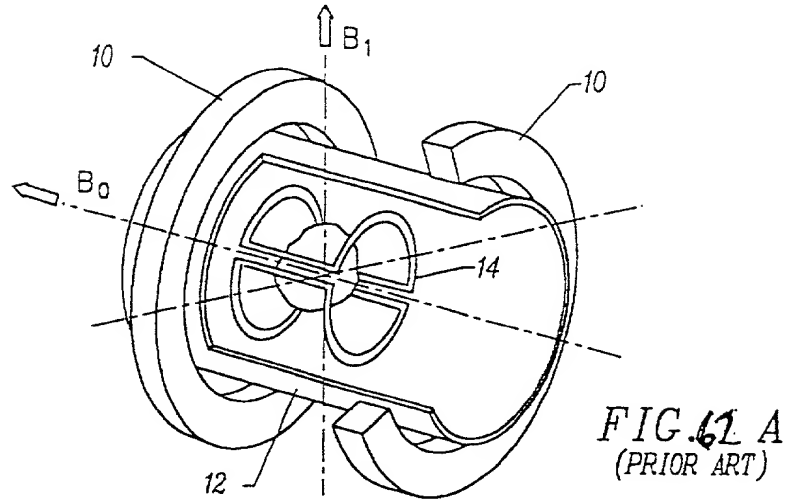
Figure SRL 60 Slices from a 3D data set of C173 showing views and scoring of an OCT graft in the medial condyle

Scoring Osteochondral (OCT) grafts from 3D MRI scans

	Sample	Filling	Integration	Surface	SC Bone	Signal	Total (max 15)
C181	G34 – Rt Knee Medial Condyle	2	1	2	1	3	9
C182	G34 – Rt Knee Lateral Condyle	2	1	2	1	3	9
C173	G33 – Rt Knee Medial Condyle	3	2	2	1	3	11
C174	G33 – Rt Knee Lateral Condyle	3	3	1	3	3	13

Figure SRL 61. Table summarising scores OCT grafts from 3-D MRI scans

FO5040" 04082860



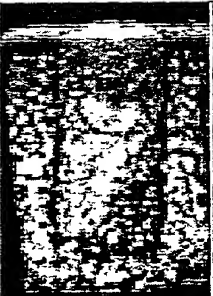
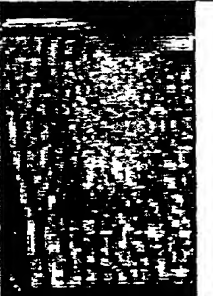


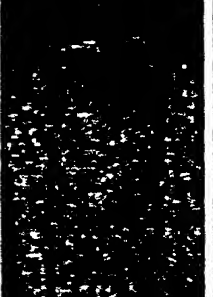
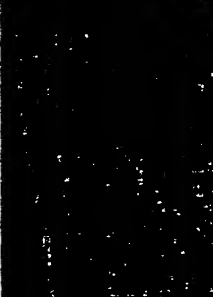










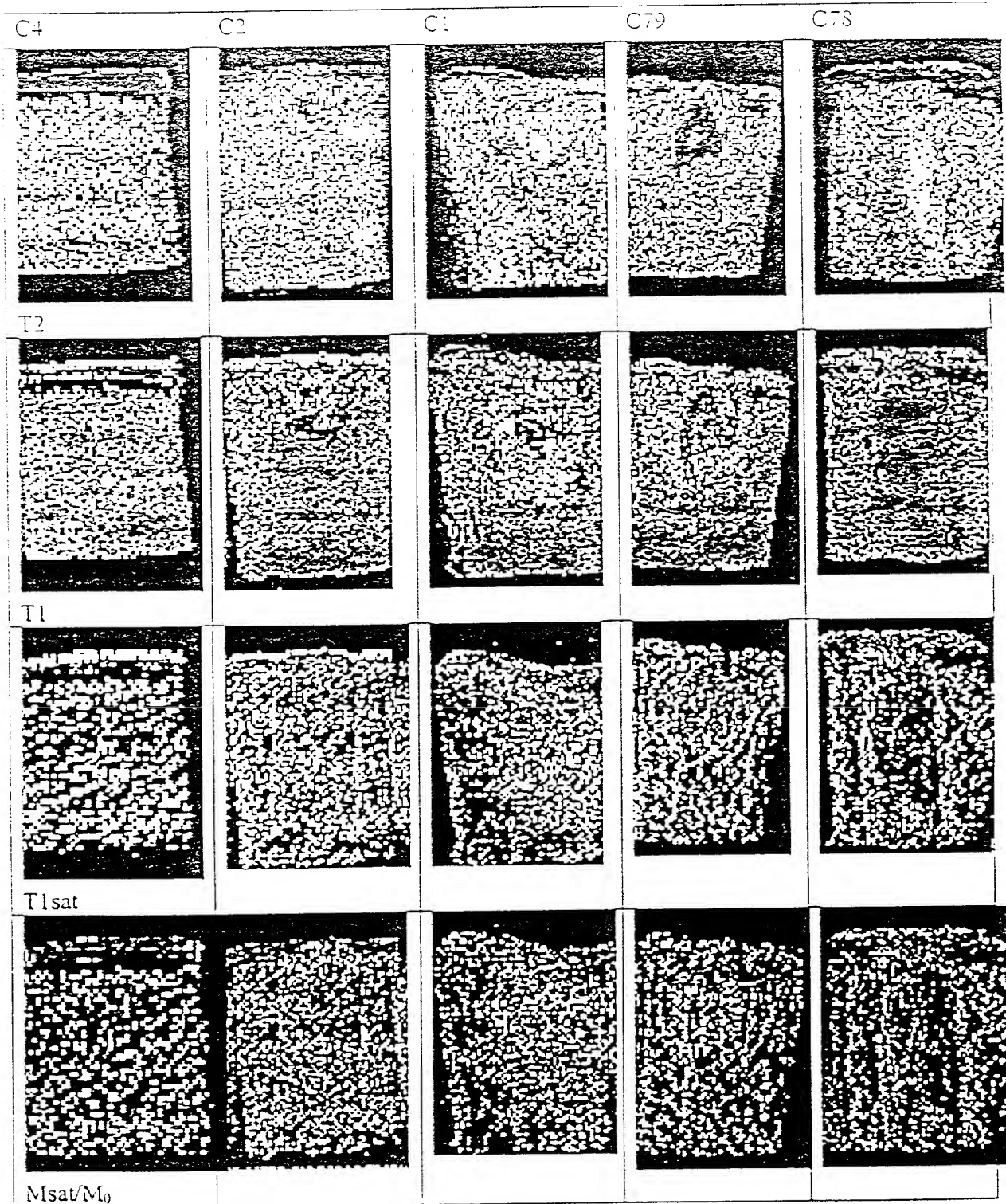
	C2	C1	C79	C78
T2 contrast (1 st echo) TR 1500ms TE 6ms				
T2 contrast (last echo) TR 1500ms TE 48ms				
T1 contrast TR 500ms TE 6ms				
MT contrast 200ms saturation				

Figure SRL 7

Selected MR scans from qMRI analysis of spontaneously healed ACD3 defects C1, C2, C78, C79 at 8 weeks.

FIG. 64A

09828070-04554
FD5040-02082860



Quantitative spatial maps of MR parameters

FIG. 64B

T2 Spatial Maps

Control cartilage (C4)

ACD3

Spontaneous Repair (C1)
matrix (C77)

ACD3

Implanted

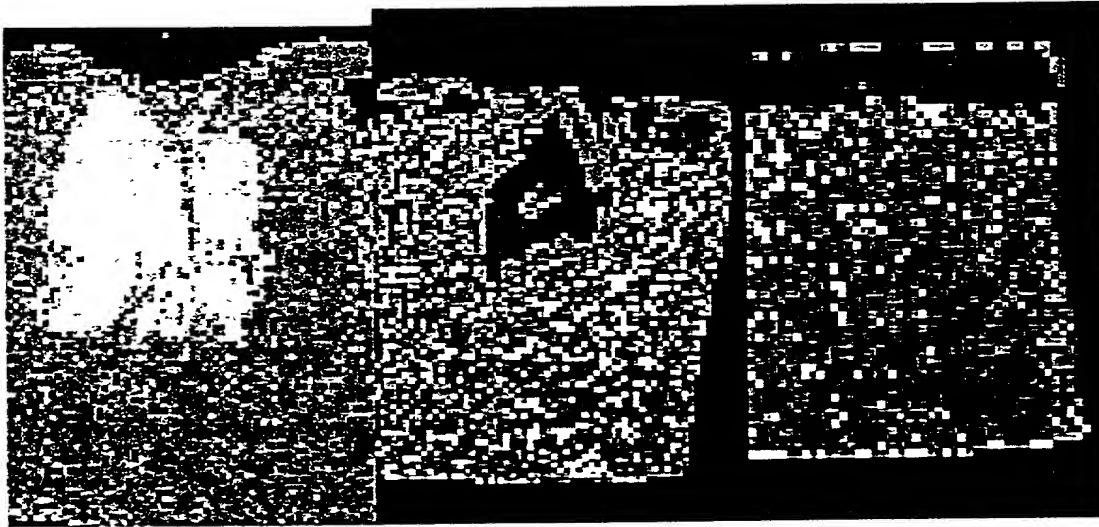






















































FIG. 64C

see Fig. SRL 2
Figs. SRL 47,48,49

~~see Figs. SRL 32 & 35~~

see

0922070.040501

T2	T1	T1sat	M1sat/M10
 1-14 (ms)	 1-249 (ms)	 1-9 (ms)	 0.01-0.09
 15-22	 250-425	 10-29	 0.1-0.18
 23-30	 426-600	 30-48	 0.19-0.26
 31-38	 601-775	 49-67	 0.27-0.34
 39-46	 776-950	 68-86	 0.35-0.42
 47-54	 951-1125	 87-105	 0.43-0.50
 55-62	 1126-1300	 106-124	 0.51-0.58
 63-70	 1301-1475	 125-143	 0.59-0.66
 71-78	 1476-1650	 144-162	 0.67-0.74
 79-86	 1651-1825	 163-181	 0.75-0.82
 87-94	 1826-2000	 182-200	 0.83-0.90
 95-1000	 2001-3000	 201-400	 0.91-0.99
 > 1000	 > 3000	 > 400	 > 0.99

Note the colour scales are different for T2 relaxation rates of clinical samples.

FIG. 65

Figure 8.8. Range of colours assigned to different qMRI values for spatial maps.

An alternative way of expressing the qMRI data is to colour each pixel according to the range of values shown above. The image can then be displayed as a quantitative spatial map for each MR parameter

for direct comparison with the histology.